EPA Jacket 11556-155

ISB'S Front-end PRIA Completeness Screen

Draft 3; 10/25/07

EPA Receipt Date: 9/24	EPA Reg. Number: 11556-RLL

	Check List Item	Yes	No	N/A
1	Has the **PRIA Fee been Paid**; is a copy of the check or Pay.gov receipt included in the Submission Package?			
2	Is an **Application Form** (EPA Form 8570-1) Included in the Submission Package, is it completely filled out and signed including package type?	X		
3	Is a **Confidential Statement of Formula** (EPA Form 8570-29) Included in the Submission Package, is it completely filled out and signed (boxes 1-21)?	X		
4	Is a **Formulator's Exemption Statement** (EPA Form 8570-27) Included in the Submission Package?		X	
5	Is a **Certification with Respect to Citation of Data** (EPA Form 8570-34) Included in the Submission Package?	X		
6	Is a **Data Matrix** (EPA Form 8570-35) Included in the Submission Package?	X		
7	Is a **Label** Included in the Submission Package?	X		
8	Are **Data** Included in the Submission Package?	X		
9	**Is the Submission an Amendment?**			

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060 Print Form

United States Environmental Protection Agency Washington, DC 20460

☐ Registration ☐ Amendment ☒ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
11556-155	Richard Gebken	☒ None ☐ Restricted
4. Company/Product (Name) PNR1427 Insecticide	**PM#** 13	

5. Name and Address of Applicant *(Include ZIP Code)*
Bayer HealthCare LLC, Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390
☐ *Check if this is a new address*

6. Expedited Review. In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☒ Notification - Explain below.
☒ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of Final Printed Labeling - No action required. ABNs: Seresto Small Dog; Seresto Large Dog. Attached are labelling proofs for product to be used specifically in the CDC Rocky Mountain Spotted Fever Pilot Prevention program. Commercial packaging for sales launch will submitted later this year.
Contact: doug.spilker@bayer.com

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☒ No	☐ Yes ☒ No	☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☒ Other (Specify) _____
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☒ Container	1 Collar	☐ On Label ☒ On Labeling accompanying product

6. Manner in Which Label Is Affixed to Product ☒ Lithograph ☐ Paper glued ☐ Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Douglas A. Spilker, Ph D.	EPA Reg. Affairs Manager	913-268-2751

Certification
I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title
Douglas A. Spilker	EPA Reg. Affairs Manager
4. Typed Name Douglas A. Spilker, Ph D.	**5. Date** 30 March 2012

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

NOT REVIEWED
In Accordance with PR Notice 82-2
Based on Draft Labeling Dated

Front Panel

Seresto ™ Small Dog

For 8 – month prevention and treatment of ticks and fleas on small dogs and puppies 7 weeks of age and older and up to 18 lbs. (8 kg)

ACTIVE INGREDIENT:	
Flumethrin; [Cyano(4 – fluoro – 3 – phenoxyphenyl)methyl 3 – [2 – chloro – 2 – (4 – chlorophenyl)ethenyl] – 2,2 – dimethylcyclopropanecarboxylate]*	**4.5%**
Imidacloprid	**10.0%**
OTHER INGREDIENTS	**85.5%**
Total	**100.0%**

***Trans Z – 1/trans Z – 2 ratio: max 66% trans Z – 1 and min 34% trans Z – 2**

Net Contents: 1 Collar 0.44 oz. (12.5 gm) per collar

EPA Reg. No. 11556 – 155 **EPA Est. No. 11556 – KS – 1**

See insert inside for additional Product Information and Directions for Use.

READ THE ENTIRE LABEL BEFORE EACH USE

DO NOT OPEN UNTIL READY TO USE
DO NOT LET CHILDREN PLAY WITH THIS COLLAR

Manufactured For:
Bayer HealthCare LLC, Animal Health Division
P.O. Box 390, Shawnee Mission, Kansas 66201 USA
Made in Germany

Mat. No.: 81544906
Batch No.: KP05KTJ
SSID: 2180

Inner Pouch

Seresto™ Small Dog

10.0% imidacloprid
4.5% flumethrin

Do not let children play with this collar
FOR USE ON DOGS

See insert for complete label information.
Do not open until ready to use.

BAYER

EPA Reg. No. 11556–155
EPA Est. No. 11556–KS–1

NOT REVIEWED
In Accordance with PR Notice 82-2
Based on Draft Labeling Dated

Front Panel

Seresto ™ Large Dog

For 8 – month prevention and treatment of ticks and fleas on large dogs and puppies 7 weeks of age and older and above 18 lbs. (8 kg)

ACTIVE INGREDIENT:	
Flumethrin; [Cyano(4 – fluoro – 3 – phenoxyphenyl)methyl 3 – [2 – chloro – 2 – (4 – chlorophenyl)ethenyl] – 2,2 – dimethylcyclopropanecarboxylate]*	**4.5%**
Imidacloprid	**10.0%**
OTHER INGREDIENTS	**85.5%**
Total	**100.0%**

***Trans Z – 1/trans Z – 2 ratio: max 66% trans Z – 1 and min 34% trans Z – 2**

Net Contents: 1 Collar 1.6 oz. (45.0 gm) per collar

EPA Reg. No. 11556 – 155 **EPA Est. No. 11556 – KS – 1**

See insert inside for additional Product Information and Directions for Use.

READ THE ENTIRE LABEL BEFORE EACH USE

DO NOT OPEN UNTIL READY TO USE
DO NOT LET CHILDREN PLAY WITH THIS COLLAR

Manufactured For:
Bayer HealthCare LLC, Animal Health Division
P.O. Box 390, Shawnee Mission, Kansas 66201 USA
Made in Germany

Mat. No.: 81544930
Batch No.: KP05KF6
SSID: 2181

Inner Pouch

Seresto™ Large Dog

10.0% imidacloprid
4.5% flumethrin

Do not let children play with this collar
FOR USE ON DOGS

See insert for complete label information.
Do not open until ready to use.

BAYER

EPA Reg. No. 11556 – 155
EPA Est. No. 11556 – KS – 1

Insert

Seresto™ Small Dog

For 8-month prevention and treatment of ticks and fleas on small dogs and puppies 7 weeks of age and older and up to 18 lbs. (8 kg)

Seresto™ Large Dog

For 8-month prevention and treatment of ticks and fleas on large dogs and puppies 7 weeks of age and older and above 18 lbs. (8 kg)

- Repels and kills ticks for 8 months, including Deer ticks, (Ixodes scapularis) vector of Lyme disease and anaplasmosis), American dog ticks, (Dermacentor variabilis) vector of Rocky Mountain spotted fever and ehrlichiosis, Brown dog ticks, (Rhipicephalus sanguineus) vector of ehrlichiosis, anaplasmosis, bartonellosis, babesiosis, canine hemoplasmosis, and Rocky Mountain spotted fever), and Lone Star ticks (Amblyomma americanum) vector of ehrlichiosis
- Prevents tick infestations within 48 hours after application
- Re-intesting ticks are repelled and/or killed as quickly as 6 hours
- Quickly kills fleas on dogs within 24 hours and continues to prevent infestations for 8 months
- Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting 8 months
- Kills fleas before they lay eggs
- Aids in control of flea larvae in the dog's surrounding
- Treatment with Seresto kills fleas and may reduce the risk of tapeworm infections (Dipytidium caninum), Bartonellosis (Bartonella vinsonii, Bartonella spp.), and Rickettsiosis (Rickettsia felis), which are types of canine vector borne diseases
- Aids in the treatment and control of Sarcoptic mange
- Make sure to replace the collar after 8 months for year-rovnd control prevention
- No need to remove collar when your pet goes swimming or gets bathed
- Water resistant
- Patented Bayer polymer matrix ensures that both active ingredients are slowly and continuously released in low concentrations

ACTIVE INGREDIENT:

Flumethrin; [Cyano(4-fluoro-3-phenoxyphenyl)methyl 3-[2-chloro- 2-(4-chlorophenyl)ethenyl) -2,2-dimethylcyclopropanecarboxylate(*	4.5%
Imidacloprid	10.0%
OTHER INGREDIENTS	85.5%
Total	100.0%

*Trans Z- t/trans Z-2 ratio: max 66% trans Z-1 and min 34% trans Z-2

EPA Reg. No. 11556-155 EPA Est. No. 11556-KS-1

READ THE ENTIRE LABEL BEFORE EACH USE
DO NOT OPEN UNTIL READY TO USE
DO NOT LET CHILDREN PLAY WITH THIS COLLAR
KEEP OUT OF REACH OF CHILDREN

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor, or going for treatment.

- For CONSUMER QUESTIONS, call 1-800-255-6826.
- For medical emergencies involving HUMANS, call 1-800-422-9874.
- For medical emergencies involving ANIMALS, call 1-800-422-9874.

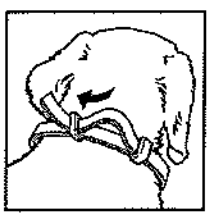
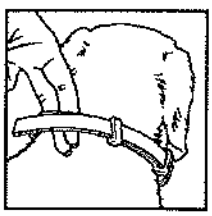
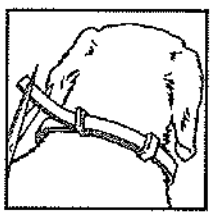
DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not contaminate feed or food.

HOW TO APPLY

One collar per animal to be fastened around the neck.

Remove collar from protective bag directly before use. Unroll collar and make sure that there are no remnants from the plastic connectors inside the collar. Insert end of the collar through the buckle. Adjust the collar around the animal's neck without tightening it too tight (as a guide, it should be possible to insert 2 fingers between the collar and the neck). Pull excess collar through the loop(s) and cut off any excess length extending beyond 1 inch (2 cm) beyond the loop(s).

The collar should be worn continuously for the 8 month protection period. Check periodically and adjust fit if necessary, especially when puppies are rapidly growing.

This collar is designed with a safety-closure mechanism. In the unlikely event of a dog being trapped, the dog's own strength is sufficient to widen the collar to allow for quick release.

Replace the collar after 8 months for optimal flea and tick protection.

PRODUCT INFORMATION

Kills fleas which may cause flea allergy dermatitis (FAD) or flea bite hypersensitivity (FBH).

Seresto kills existing fleas on dogs within 24 hours. Reintesting fleas are killed within 2 hours with protection against further flea infestation lasting eight (8) months. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions. Seresto aids in the control of flea larvae in the dog's surroundings following contact with a Seresto-treated dog.

Ticks already on the dog prior to treatment may not be killed immediately after collar application and may remain attached and visible. At the time of application remove ticks already on the dog. The prevention of infestations with new ticks starts within 48 hours after application of the collar. Re-infesting ticks are repelled and/or killed as quickly as 6 hours.

Aids in the treatment and control of Sarcoptic mange.

Seresto is water resistent and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight. Under normal conditions, effectiveness lasts for 8 months. In order to maintain an eight-month duration, dogs must not be bathed more than once per month. For dogs that swim once a month or more, the control duration is reduced to 5 months. In case of loss of collar, a new collar may be applied immediately.

Occasionally slight itching may be observed in animals that are not used to wearing collars in the first few days after fitting. Ensure that the collar is not fitted too tightly. Slight hair loss and mild skin reactions due to the mechanical irritation of the collar may occur at the application site which usually recover within 1 or 2 weeks without the need for collar removal. If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinarian.

Do not attach a leash to the collar as this may cause breakage.

Keep the collar in the bag and in the outer packaging until use. As with any pesticide product, do not allow small children to play with the collar or to put them into their mouths. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and cold water after fitting the collar. People with sensitivity reactions to the ingredients of the collar should avoid contact with the collar. Do not place collar in mouth. Not intended for use on humans.

For external use on dogs only. Do not use on other animals. Do not use on puppies under seven weeks of age. Do not get this product in dog's eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, breeding, pregnant, or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs of sensitivity occur remove collar and bathe your pet with mild soap and rinse with large amounts of water. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. If your dog is experiencing an adverse event, contact your veterinarian and, call 1-800-422-9874.

The patented Bayer polymer matrix system ensures that both active ingredients are slowly and continuously released in low concentrations from the collar towards the animal. This avoids peak concentrations and ensures that concentrations of both active ingredients are present in the dog's haircoat during the entire efficacy period. The active ingredients spread from the site of direct contact over the entire skin surface.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in original unopened container in a cool, dry place that is inaccessible to children.

Container Disposal: Dispose of container, pouch and expired collar in trash.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division, warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. To the extent consistent with applicable law any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc.

Bayer (reg'd), the Bayer Cross (reg'd), and Seresto are trademarks of Bayer.

Manufactured For
Bayer HealthCare LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, Kansas 66201 USA
Made in Germany

81544906
81544930
t6720

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (H7505C)
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

EPA Reg. Number:	Date of Issuance:
11556-155	MAR 16 2012

Term of Issuance: Unconditional

Name of Pesticide Product: PNR1427 Insecticide

NOTICE OF PESTICIDE:
X Registration
___ Reregistration

(Under FIFRA as amended)

Name and Address of Registrant (include ZIP Code):
Bayer HealthCare LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered/reregistered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is **unconditionally** registered in accordance with FIFRA sec. 3(c)(5) for a period of one year from the date of registration. This registration will expire on March 17, 2013.

Once a pesticide is registered, however, it is not regarded as permanently acceptable. Registration does not eliminate the need for continual reassessment of pesticides. If the Agency determines that, at any time, additional data are required to maintain in effect an existing registration, the Agency will require submission of such data under FIFRA section (3).

1. You will make the following label changes before you release the product for shipment:

   a) Revise the EPA Registration Number to read "EPA Reg. No. 11556-155."

   b) Replace the following claim: "For 8-month prevention and treatment of ticks, fleas, and lice on … etc" with "For 8-month prevention and treatment of ticks and fleas on … etc". Also replace "Replace the collar after 8 months for (optimal) (continuous) flea, (lice) and tick protection" with "Replace the collar after 8 months for (optimal) (continuous) flea, and tick protection". All claims related to "8 months" must be limited to fleas and ticks only. Other pests are not controlled for that duration.

   c) Claims against lice must be limited to one month.

   d) Tick claims for killing within 6 hours of re-infestation on cats must be removed from the label. Based on the submitted or cited data the claim only is supported for dogs.

Signature of Approving Official:
Wanda Alexander for
Richard Gebken Product Manager
Insecticide Branch/Registration Division (7505P)

Date: March 16, 2012

Enclosure

e) All waterproof claims must be clarified as follows:

- In order to maintain an eight month control duration, dogs must not be bathed more than once per month.
- If dogs swim once per month, the control duration must be revised to 5 months.
- Water exposure (i.e. immersion, bathing, or prolonged exposure to rain) can only be once per month.

f) On page 2 delete the directions for killing roaches and ants (in the environment").

g) All claims related to control of flea larvae in the pet's environment must be removed or revised to "aids on control" for fleas in the pet's environment.

h) All disease claims must be deleted, unless the claim is stated "kills/controls xxx pest that may vector yyy".

i) All claims of "breaking the flea life cycle" must be deleted.

2. Please submit three (3) copies of your final printed labeling before releasing the product for shipment. If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA section 6(e). Your release for shipment of the product bearing amended labeling constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

If you have any questions regarding this action, please contact BeWanda Alexander at www.alexander.bewanda@epa.gov or (703) 305-7460.

Note to Reviewer: Brackets [ ] and parentheses ( ) denote optional language

PNR1427 Insecticide

Alternate Brand Names: Seresto Small Dog; Seresto Large Dog; Seresto Cat

Optional Language for Small Collar

[For 8-month prevention and treatment of ticks, fleas, and lice on (small) dogs and puppies 7 weeks of age and older and up to [(18 lbs.)(8 kg)] [body weight]]

-or-

[For 8-month prevention and treatment of ticks and fleas on cats and kittens 10 weeks of age and older]

-or-

[For 8-month prevention and treatment of ticks, fleas, and lice on (small) dogs and puppies 7 weeks of age and older and up to [(18 lbs.)(8 kg)] [body weight]] [and/or] prevention and treatment of ticks and fleas on cats and kittens 10 weeks of age and older]

Optional Language for Large Collar:

[For 8-month prevention and treatment of ticks, fleas and lice for 8 months on (large) dogs and puppies 7 weeks of age and older and above [(18 lbs.)(8 kg)] [body weight]]

- [Selected optional label claims bulleted here from pages 9 to 15]
-

ACTIVE INGREDIENT:	
Flumethrin; [Cyano(4-fluoro-3-phenoxyphenyl)methyl 3-[2-chloro- 2-(4-chlorophenyl)ethenyl] -2,2-dimethylcyclopropanecarboxylate]*	4.5%
Imidacloprid	10.0%
OTHER INGREDIENTS	85.5%
Total	100%

*Trans Z-1/trans Z-2 ratio: max 66% trans Z-1 and min 34% trans Z-2

Net Contents: (X) Collar (s) – XX oz. (XX grams) per collar	
EPA Reg. No. 11556-XXX	**EPA Est. No. 11556-TBD**

Manufactured For

Bayer HealthCare LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, Kansas 66201 USA

Made in Germany

READ THE ENTIRE LABEL BEFORE EACH USE

[For small collar: USE ON [(DOGS)(CATS)]]
-or-
[For small collar: USE ON SMALL DOGS and CATS]
-or-
[For large collar: USE ONLY ON DOGS]

DO NOT OPEN UNTIL READY TO USE
DO NOT LET CHILDREN PLAY WITH THIS COLLAR [OR REFLECTORS]

KEEP OUT OF REACH OF CHILDREN
[CHOKING HAZARD - CONTAINS SMALL PARTS]

See [(back panel)(insert)] for additional Product Information and Directions for Use.

HOT LINE NUMBER
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. • For CONSUMER QUESTIONS, call 1-800-255-6826. • For medical emergencies involving HUMANS, call 1-800-422-9874. • For medical emergencies involving ANIMALS, call 1-800-422-9874.

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not contaminate feed or food.

HOW TO APPLY

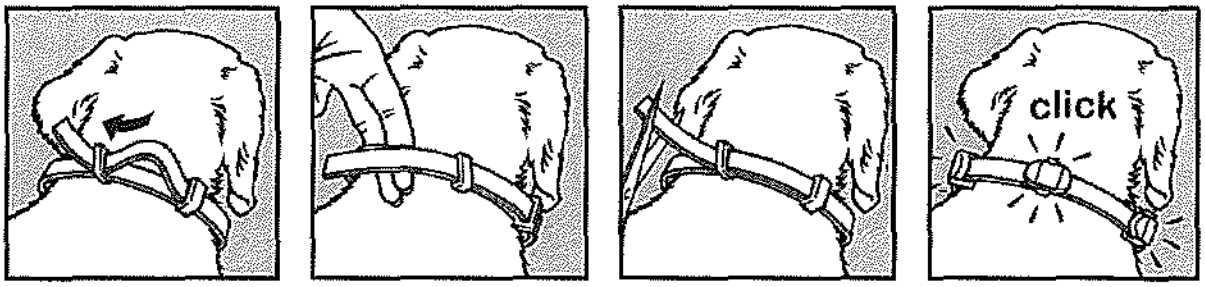
One collar per animal to be fastened around the neck.

Remove collar from protective bag directly before use. Unroll collar and make sure that there are no remnants from the plastic connectors inside the collar. Insert end of the collar through the buckle. Adjust the collar around the animal's neck without tightening it too tight (as a guide, it should be possible to insert 2 fingers between the collar and the neck). Pull excess collar through the loop(s) and cut off any excess length extending beyond (1/one/an) inch (2 cm) beyond the loop(s).

[After application of the collar, three reflector clips may be fixed permanently to the collar to increase the animal's visibility in the dark. Take the clips out of the bag. The clips should be evenly distributed on the non-overlapping part of the collar. The clips are correctly applied when a clicking sound is heard. For safety reasons once the reflectors are fixed to the collar the clasp closes permanently and cannot be re-opened.]

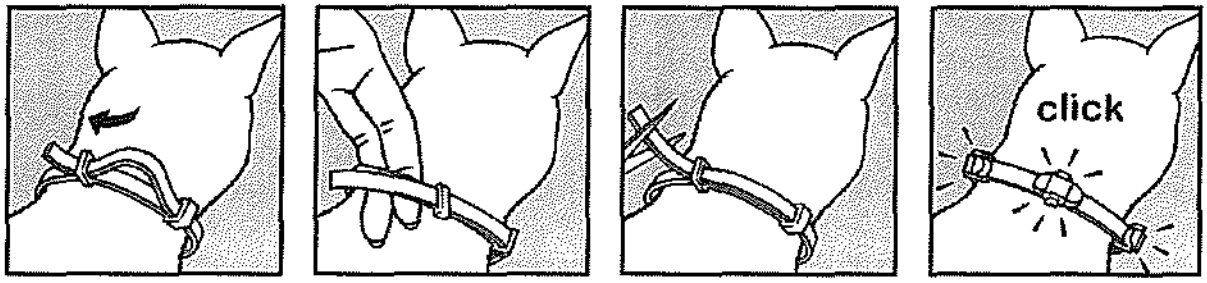
[Optional Visuals:

Dog



- or -

Cat



The collar should be worn continuously for the 8 month protection period. Check periodically and adjust fit if necessary, especially when [(puppies)(kittens)] are rapidly growing.

This collar is designed with a safety-closure mechanism. In the unlikely event of a [(dog)(cat)(pet)] being trapped, the [(dog's)(cat's)(pet's)] own strength is sufficient to widen the collar to allow for quick release.

Replace the collar after 8 months for (optimal) (continuous) flea, (lice) and tick protection.

PRODUCT INFORMATION

Kills fleas which may cause flea allergy dermatitis (FAD) or flea bite hypersensitivity (FBH).

[(PNR 1427 Insecticide)(Brandname)(This product)(The collar)] kills existing fleas on [(dogs)(cats)] within 24 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting eight (8) months. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Larval flea stages in the [(dog's)(cat's)] surroundings are killed following contact with a [(PNR 1427 Insecticide)(brand name)]-treated [(dog)(cat)].

Ticks already on the [(dog)(cat)] prior to treatment may not be killed immediately after collar application and may remain attached and visible. At the time of application remove ticks already on the [(dog)(cat)]. The prevention of infestations with new ticks starts within 48 hours after application of the collar.

Re-infesting ticks are [(repelled)(killed)(repelled and/or killed)] as quickly as 6 hours.

(Kills lice on dogs.)
Aids in the treatment (and control) of Sarcoptic mange.

[(PNR 1427 Insecticide)(Brand name)(This product)(The collar)] is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight. Under normal conditions, effectiveness lasts for 8 months. In case of loss of collar, a new collar may be applied immediately.

Occasionally slight itching may be observed in animals that are not used to wearing collars in the first few days after fitting. Ensure that the collar is not fitted too tightly. Slight hair loss and mild skin reactions due to the mechanical irritation of the collar may occur at the application site which usually recover within 1 or 2 weeks without the need for collar removal. If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinarian.

Do not attach a leash to the collar as this may cause breakage.

Keep the collar in the bag and in the outer packaging until use. As with any pesticide product, do not allow small children to play with the collar (or reflectors,) or to put them into their mouths. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and cold water after fitting the collar. People with sensitivity reactions to the ingredients of the collar should avoid contact with the collar. [Choking hazard. Contains small parts]. Do not place collar [or reflectors] in mouth. Not intended for use on humans.

For external use on [(dogs)(and)(cats)] only. Do not use on other animals. [(Do not use on puppies under seven weeks of age.)(Do not use on kittens under ten (10) weeks of age.)] Do not get this product in [(dog's)(cat's)] eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, breeding, pregnant, or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for pets. If signs of sensitivity occur remove collar and bathe your pet with mild soap and rinse with large amounts of water. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product. If your [(dog)(or)(cat)] is experiencing an adverse event, contact your veterinarian and, call 1-800-422-9874.

The patented Bayer polymer matrix system ensures that both active [(substances)(ingredients)] are slowly and continuously released in low concentrations from the collar towards the animal. This avoids peak concentrations and ensures that concentrations of both

active [(substances)(ingredients)] are present in the [(cat's)(and/or)(dog's)] haircoat during the entire [(protection)(efficacy)] period. The active [(substances)(ingredients)] spread from the site of direct contact over the entire skin surface.

[INSERT DIAGRAM THAT DEPICTS RELEASE FROM MATRIX.]

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.
Pesticide Storage: Store in original unopened container in a cool, dry place that is inaccessible to children.
Container Disposal: Dispose of container, pouch and expired collar in trash.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Bayer HealthCare LLC, Animal Health Division, warrants that this material conforms to the chemical description on the label. TO THE EXTENT CONSISTENT WITH APPLICABLE LAW, BAYER MAKES NO OTHER EXPRESS OR IMPLIED WARRANTY, INCLUDING ANY OTHER EXPRESS OR IMPLIED WARRANTY OF FITNESS OR MERCHANTABILITY, and no agent of Bayer is authorized to do so except in writing with a specific reference to this warranty. To the extent consistent with applicable law any damages arising from a breach of this warranty shall be limited to direct damages and shall not include consequential commercial damages such as loss of profits or values, etc. [The reflector clips contained herein are only meant to be used in combination with the specific collar and have been tested only for such use and purpose. To the extent consistent with applicable law, Bayer excludes liability for any misuse and use other than in combination with the specific collar as described in the packaging leaflet.]

Pouch Label

[(PNR 1427 Insecticide)(Brand name)]

10.0% imidacloprid
4.5% flumethrin

Do not let children play with this collar (or reflectors).
FOR USE ON (CATS)(DOGS)(CATS & DOGS)
See (outer container/leaflet) for complete label information.
Do not open until ready to use.

BAYER

EPA Reg. No. 11556-XXXX
EPA Est. No. 11556-TBD

Lot No. 0000000

Note to Reviewer: Brackets [ ] and parentheses ( ) denote optional language

Optional/Alternative Marketing Claims – Dogs

General Claims - Dogs

- Two active [(substances)(ingredients)] provide dual action against ticks, fleas, and lice (on dogs)
- For use on dogs and puppies 7 weeks of age and older
- Tick, (and) flea (and lice) (prevention)(control)(and) treatment for dogs 7 weeks of age or older
- [(PNR 1427)(Brand name)(This product)] is indicated for the prevention and treatment of ticks, fleas and lice on dogs and puppies (7 weeks of age and older)
- [Effective][Long-lasting] [protection] for 8 months
- Kills (and repels) ticks, (and) kills fleas (and lice)(for 8 months)
- Reliable 8-month protection against ticks, fleas, and lice on dogs (and puppies)
- [3-way] protection against fleas, ticks and lice
- 8-month protection against ticks, fleas and lice
- For (small) dogs up to [(18 lbs.)(8 kg)] [body weight]
- For (large) dogs above [(18 lbs.)(8 kg)] [body weight]
- For external use on dogs
- For [(small dogs and puppies)(large dogs)]
- Fully effective within 48 hours after initial application of collar

Tick Claims - Dogs

- Repels and kills ticks, including [(Deer)(Black-legged)] ticks, (*Ixodes scapularis)* (vector of Lyme disease and anaplasmosis), American dog ticks, (*Dermacentor variabilis)* (vector of Rocky Mountain spotted fever and ehrlichiosis), Brown dog ticks, (*Rhipicephalus sanguineus)* (vector of ehrlichiosis, anaplasmosis, bartonellosis, babesiosis, canine hemoplasmosis, and Rocky Mountain spotted fever), and Lone Star ticks (*Amblyomma americanum)* (vector of ehrlichiosis) for 8 months
- Treatment with [(PNR 1427)(brand name)(this product)(the collar)] kills ticks that may transmit Anaplasmosis (*Anaplasma phagocytophilium*), Bartonellosis (*Bartonella vinsonii, Bartonella spp.*), Babesiosis (*Babesia canis, B. gibsoni*), Borreliosis (*Borrelia burgdorferi*), canine hemoplasmosis (*Mycoplasma haemocanis*), Ehrlichiosis (*Ehrlichia canis, E. chaffeensis, E. ewingii*), Hepatozoonosis (*Hepatozoon canis* and *H. americanum*), and Rickettsiosis (*Rickettsia rickettsii*) [,which are types of (canine) vector borne diseases]
- Efficacy against ticks (by repelling and killing) that may transmit Anaplasmosis (*Anaplasma phagocytophilium*), Bartonellosis (*Bartonella vinsonii, Bartonella spp.*),

Babesiosis (*Babesia canis, B. gibsoni*), Borreliosis (*Borrelia burgdorferi*), canine hemoplasmosis (*Mycoplasma haemocanis*), Ehrlichiosis (*Ehrlichia canis, E. chaffeensis, and E. ewingii*), Hepatozoonosis (*Hepatozoon canis* and *H. americanum*), and Rickettsiosis (*Rickettsia rickettsii*) [,which are types of (canine) vector borne diseases]

- Kills [(Deer)(Black-legged)] ticks (, which may carry Lyme disease and Anaplasmosis)
- Kills American dog ticks (, which may carry Rocky Mountain spotted fever and Ehrlichiosis)
- Kills all [(life)(blood feeding)] stages of ticks
- Kills tick adults, larvae, and nymphs
- Kills ticks within 48 hours of (intitial) application
- Prevents tick infestations within 48 hours after (inititial) application
- [(Kills)(Repels)] ticks in 6 hours after (intial) efficacy has been obtained
- Re-infesting ticks are [(repelled)(killed)(repelled and/or killed)] as quickly as 6 hours
- Protects against all types of ticks (attacking dogs)
- Protects your (dog)(and/or)(puppy) from all types of ticks (for 8 months)
- Easy, effective [(treatment and prevention)(control)] of ticks, (and) fleas (,and lice)

Flea Claims - Dogs

- (Rapidly/Quickly]) Kills fleas on dogs within [24] hours and continues to prevent infestations for 8 months
- Kills fleas before they lay eggs
- Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting 8 months
- Larval flea stages in the dog's surroundings are killed following contact with a [(PNR 1427)(brand name)] -treated dog, (which will aid in environmental control)
- Prevents, treats, and controls flea larvae in the dog's immediate surroundings
- Prevents, treats, and controls adult and larval stages of the flea
- Protects your (dog)(and/or)(puppy) from fleas (for 8 months)
- For the treatment and prevention of flea infestations [on your dog (and in your dog's immediate surroundings)]
- One treatment prevents further flea infestations (on dogs) for 8 months
- Controls existing flea infestations by killing adult fleas
- Prevents reinfestations by killing adult fleas before they lay eggs
- Prevents fleas on treated dogs from infesting (reinfesting) your home
- Treatment with [(PNR 1427)(brand name)(this product)(the collar)] kills fleas and may reduce the incidence of [flea allergy dermatitis (FAD)][flea bite hypersensitivity (FBH)][flea bite dermatitis (FBD)]
- For prevention and treatment of flea infestation(s) for 8 months

- [8-month] prevention and treatment of cat fleas (*Ctenocephalides felis),* dog fleas *(Ctenocephalides canis)* and human fleas *(Pulex irritans*) on dogs
- Kills cat fleas (*Ctenocephalides felis,)* dog fleas *(Ctenocephalides canis)* and human fleas *(Pulex irritans*) on dogs
- Treatment with [(PNR 1427)(brand name)(this product)(the collar)] kills fleas and may reduce the (risk/incidence) of tapeworm infections (*Dipylidium caninum*), Bartonellosis (*Bartonella vinsonii, Bartonella spp.*), and Rickettsiosis (*Rickettsia felis*) [,which are types of (canine) vector borne diseases]
- Efficacy against fleas that may transmit tapeworm infections (*Dipylidium caninum*), Bartonellosis (*Bartonella vinsonii, Bartonella spp.*), and Rickettsiosis (*Rickettsia felis*) [,which are types of (canine) vector borne diseases]
- Breaks the flea life cycle
- Stops fleas from feeding by (their) paralysis and death
- Kills fleas that may cause anemia in dogs

Lice & Other Efficacy Claims - Dogs

- Kills [(biting) (chewing)] lice
- For treatment and prevention of [(biting) (chewing)] lice (infestations)
- Controls existing [(biting) (chewing)] lice infestations
- Treats, prevents and controls [(biting) (chewing)] lice (infestations)
- Provides effective control of [(biting) (chewing)] lice (infestations)
- Kills [(biting) (chewing)] lice and prevents further infestations
- For treatment and prevention of infestations of [(biting) (chewing)] lice
- Aids in the treatment (and control) of Sarcoptic mange

Optional/Alternative Marketing Claims – Cats

General Claims - Cats

- Two active [(substances)(ingredients)] provide dual action against ticks and fleas (on cats)
- For use on cats and kittens 10 weeks of age and older
- [Effective][Long-lasting] [protection] for 8 months
- Tick, (and) flea (prevention)(control)(and) treatment for kittens 10 weeks of age or older
- Tick and flea treatment for cats and kittens 10 weeks of age and older
- [(PNR 1427)(Brand name) (The collar)(This product)] is indicated for the prevention and treatment of ticks and fleas on cats and kittens (10 weeks of age and older)
- Kills (and repels) ticks and kills fleas (for 8 months)
- (Reliable) (8-month) protection against ticks and fleas [on cats (and kittens)]
- [Dual] [2-way] protection against ticks and fleas

- For external use on cats
- For cats and kittens
- Fully effective within 48 hours after initial application of collar

Tick Claims - Cats

- Repels and kills ticks, including [(Deer)(Black-legged)] ticks, *(Ixodes scapularis)* (vector of Lyme disease and anaplasmosis), American dog ticks (*Dermacentor variabilis)* (vector of Rocky Mountain spotted fever, cytauxzoonosis, and ehrlichiosis), Brown dog ticks, (*Rhipicephalus sanguineus)* (vector of ehrlichiosis, anaplasmosis, babesiosis, and Rocky Mountain spotted fever), and Lone Star ticks (*Amblyomma americanum)* (vector of cytauxzoonosis and ehrlichiosis) (for 8 months)
- Treatment with [(PNR 1427)(brand name)(this product)(the collar)] kills ticks that may transmit Anaplasmosis (*Anaplasma phagocytophilium*), Babesiosis (*Babesia canis, B.spp.*), Borreliosis (*Borrelia burgdorferi*), Ehrlichiosis (*Ehrlichia canis, E. spp.*), Cytauxzoonosis (*Cytauxzoon felis*), and Rickettsiosis (*Rickettsia rickettsii*) [,which are types of (cat) vector borne diseases]
- Efficacy against ticks (by repelling and killing) that may transmit Anaplasmosis (*Anaplasma phagocytophilium*), Babesiosis (*Babesia canis, B. spp.*), Borreliosis (*Borrelia burgdorferi*), Ehrlichiosis (*Ehrlichia canis, E. spp.*), Cytauxzoonosis (*Cytauxzoon felis*), and Rickettsiosis (*Rickettsia rickettsii*) [,which are types of (cat) vector borne diseases]
- Kills [(Deer)(Black-legged)] ticks (, which may carry Lyme disease)
- Kills American dog ticks (, which may carry Rocky Mountain spotted fever)
- Kills all (life) (blood feeding) stages of ticks
- Kills tick adults, larvae, and nymphs
- Kills ticks within 48 hours of (intitial) application
- Prevents tick infestations within 48 hours after (initial) application
- [(Kills)(Repels)] ticks in 6 hours after (intitial) efficacy has been obtained
- Re-infesting ticks are [(repelled)(killed)(repelled and/or killed)] as quickly as 6 hours
- Protects against all types of ticks (attacking cats)
- Protects your (cat)(and/or)(kitten) from all types of ticks (for 8 months)
- Easy, effective [(treatment and prevention)(control)] of ticks and fleas

Flea Claims - Cats

- (Rapidly/Quickly) Kills fleas on cats within [24] hours and continues to prevent infestations (for 8 months)
- Kills and repels fleas before they lay eggs

- Reinfesting fleas are killed within 2 hours with protection against further flea infestation (lasting 8 months)
- Larval flea stages in the cat's surroundings are killed following contact with a [(PNR 1427)(brand name)(collar)] -treated cat (which will aid in environmental control)
- Prevents, treats, and controls flea larvae in the cat's immediate surroundings
- Prevents, treats, and controls adult and larval stage of the flea
- Protects your (cat)(and/or)(kitten) from fleas (for 8 months)
- For the treatment and prevention of flea infestations on your cat (and in your cat's immediate surroundings)
- One treatment prevents further flea infestations (for 8 months)
- Controls existing flea infestations by killing adult fleas
- Prevents reinfestations by killing adult fleas before they lay eggs
- Treatment with [(PNR 1427)(brand name)(the collar)(this product)] kills fleas and may reduce the incidence of [flea allergy dermatitis (FAD)][flea bite hypersensitivity (FBH)][flea bite dermatitis (FBD)]
- For prevention and treatment of flea infestation(s) for 8 months
- [8-month] prevention and treatment of cat fleas *(Ctenocephalides felis),* dog fleas *(Ctenocephalides canis)* and human fleas *(Pulex irritans)* on cats
- Treatment with [(PNR 1427)(brand name) (the collar)(this product)] kills fleas that may transmit Bartonellosis (*Bartonella henselae*), tapeworm infections (*Dipylidium caninum*), Feline infectious anemia (*Mycoplasma spp.*), and Rickettsiosis (*Rickettsia felis*)
- Efficacy against fleas that may transmit Bartonellosis (*Bartonella henselae*), tapeworm infections (*Dipylidium caninum*), Feline infectious anemia (*Mycoplasma spp.*), and Rickettsiosis (*Rickettsia felis*)
- Breaks the flea life cycle
- Stops fleas from feeding by (their) paralysis and death
- Kills fleas that may cause anemia in cats

Other Efficacy Claims - Cats

- Aids in the treatment (and control) of Sarcoptic mange

Optional/Alternative Marketing Claims – General

- Protects for 8 months
- (8-month) [(protector band)(pet collar)(collar)]
- [(Kills)(Protects)] for 8 months
- (Make sure to) replace (the) collar after 8 months [for year-round (control)(prevention)]
- Remains effective after bathing or swimming

- Remains effective following shampooing, swimming or after rain
- [(Wetness)(Moisture)] does not reduce the collar's effectiveness
- No need to remove (the) collar while bathing pet
- No need to remove collar when (your) pet goes swimming or [(gets bathed)(bathing)]
- Waterproof
- Water resistant
- Fragrance-free
- Odorless
- No (noticeable) odor
- Non-greasy
- Easy to use
- (Easy)(convenient)(to use)(to apply)
- [(Graphite)(Gray)][Red][Yellow][(collar)(color)]
- (Adjustable)(convenient)(easy-to-apply) collar
- (Light) reflectors for added visibility (in the evening and at night)
- (Three) (3) (visibility) reflectors (included)
- (Snap-on) reflectors (included) for added (night-time)(pet)(visibility)
- One collar per animal (to be fastened around the neck)
- Contains one collar
- [(Patented)(Bayer)(technology) (polymer)(matrix)(system)] ensures that both active [(substances)(ingredients)] are (slowly) (and continuously) released (in low concentrations).
- (Patented) (Bayer) (Polymer) Matrix: [(effective)(dependable)(long-lasting)] (flea and tick) control (for 8 months)
- (Depot effect:) [Active (substances)(ingredients)] stored inside the polymer matrix and gradually released over time]
- [(Continuous)(Even distribution)(Steady)] release) of active [(substances)(ingredients)] (over 8 months)
- (Continuous) protection (over 8 months)
- Contains [(Patented)(Bayer) (polymer)(matrix)(system)]

Optional/Alternative Marketing Claims – Combined label for small collar for use on small dogs and cats

- For external use on small dogs and cats only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: BeWanda Alexander

From: Clayton Myers, Entomologist Date: March 14, 2012

3-14-12

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD

DP barcode:	385561, 385623, 393362
Decision no.:	440307
Submission no:	882827, 902307
Action code:	R110.0
Product Name:	PNR 1427 Insecticide
EPA Reg. No or File Symbol:	11556-RLL
Formulation Type:	RTU Pet Collar

Ingredients statement from the label with PC codes included: Flumethrin, 4.50% PC: 36007; Imidacloprid, 10.00%, PC: 129099

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 as appropriate): One collar per animal, cut to fit with some slack around neck (varies somewhat upon animal size). Claims through 8 months for some pests, including waterproof/washing/water immersion.

I. Action Requested: Data was submitted to support pest claims for a ready to use, indoor, non-food product; a companion animal collar impregnated with 2 active ingredients.

II. Background: The registrant seeks to register a flumethrin/imidacloprid combo pet collar product for control of fleas and ticks and lice on dogs, and fleas and ticks on cats. The registrant has submitted 20 studies to support efficacy claims.

III. MRID Summaries: (Primary Review attached)

a. **MRID 48576501**

(1) GLP study

(2) A laboratory study was conducted to evaluate killing efficacy of the test product against Deer ticks, *Ixodes scapularis* adults and nymphs against hair taken from treated animals via an *in vitro* exposure study. Three dogs were acclimated and used for this study, with 2 animals provisioned with the treated collars (one as a backup), and one left as an untreated control. Pre-treatment hair samples were taken and tick exposures conducted to confirm no insecticidal activity of untreated hair. Periodically after treatment, through 240 days (8 months), hair samples were taken from the test dog and control dog from various body surfaces. One gram of hair was placed into each of 6 Petri dishes to which were added 10 nymph and 10 adult ticks. Counts of live and dead ticks were made after 48 hours of exposure. Mortality was calculated using Abbott's formula.

(3) Efficacy for all exposures and all tick stages exceeded 97% through 240 days after initial placement of the collar, with most of the exposures resulting in 100% control. Authors conclude

that efficacy is supported for Deer ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims Deer ticks, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Deer ticks, *Ixodes scapularis*, on dogs, with control starting within 48 hours of collar placement.

b. **MRID 48576502**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against Deer ticks, *Ixodes scapularis* adults on dogs treated with the collar. Dogs were acclimated and pre-qualified for tick retention. 16 dogs were used in the study with 8 each (4 males and 4 females) allocated to either a treatment or control group. 50 ticks were placed on each dog one day prior to placement of collars. Dogs under 18 lbs received a small collar and larger dogs received the large collar. Ticks were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 247 days (8 months). Mortality was calculated using Abbott's formula.
(3) Efficacy for all exposures and all tick stages exceeded 96% through 247 days after initial placement of the collar, with most of the exposures resulting in 100% control. Authors conclude that efficacy is supported for Deer ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims Deer ticks, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Deer ticks, *Ixodes scapularis*, with control starting within 48 hours of collar placement.

c. **MRID 48240116**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Dermacentor variabilis* and *Rhipicephalus sanguineus* ticks and *Ctenocephalides felis* fleas on dogs treated with the collar. Dogs were acclimated and pre-qualified for flea retention. 16 dogs were used in the study with 8 each (4 males and 4 females) allocated to either a treatment or control group. 50 ticks of each species and 100 fleas were placed on each dog one day prior to placement of collars. All dogs were over 18 lbs. and thus, all dogs received the large collar. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 254 days (8 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for all exposures exceeded 96% through 246 days after initial placement of the collar. Flea efficacy upon the day 7 re-infestation was also greater than 90% within 2 hours of re-infestation. Tick efficacy for both species exceeded 90% through 240 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the dogs hair initially). Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for American Dog Ticks, Brown Dog Ticks, and Fleas, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of dogs kept indoors.
(4) The study is acceptable to 8 month control claims against Ticks (ABT and BDT) and fleas, with control starting within 48 hours of collar placement for fleas.

d. **MRID 48240117**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Amblyomma americanum* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 16 domestic short-hair cats were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. 50 ticks and 100 fleas were placed on each cat one day prior to placement of collars. Ticks and fleas were

counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 246 days (8 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for all exposures exceeded 90% through 246 days after initial placement of the collar (8 months). Flea efficacy upon the day 7 re-infestation was also greater than 90% within 2 hours of re-infestation. Tick efficacy exceeded 90% through 240 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the cats' hair initially). Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Lone Star Ticks, and Fleas, but noted that the collars were not exposed to any weathering and thus the claims were only supportive of cats kept indoors.
(4) The study is acceptable to 8 month control claims against *Amblyomma americanum* and fleas on cats, with control starting within 48 hours of collar placement for fleas.

e. **MRID 48240118**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *R. sanguineus* and *D. variabilis* adult ticks and *Ctenocephalides felis* fleas on dogs treated with the collar after water immersion and shampooing. Dogs were acclimated and pre-qualified for flea retention. 32 dogs were used in the study with 8 each allocated to 4 groups: Treated immersed, Treated shampooed, Untreated immersed, Untreated shampooed. Shampooing was conducted monthly and the immersion group was immersed in water monthly. 50 ticks of each species and 100 fleas were placed on each dog at times prior to placement of collars. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 232 days (7 months). Mortality was calculated using Abbott's formula.
(3) Flea efficacy for the shampoo group exceeded 90% through day 225. For water immersion, efficacy only exceeded 90% though day 141. *R. sanguineus* efficacy exceeded 90% though day 232 for both groups. *D. variabilis* efficacy exceeded 90% though day 225 for shampooing but only day 197 for water immersion. The primary reviewer concurred with the author's conclusion that data was adequate to support 8 month claims for prevention of fleas and ticks when shampooed once per month. Because *D. variabilis* efficacy was only adequate for 7 months and flea efficacy was only adequate through day 141, only a 5 month claim would be acceptably supported. The reviewer also states that the label must specify that bathing/swimming should be no more than once per month for the claims to be supported by this data set.
(4) The study is acceptable to support 8 month claims against fleas and ticks for dogs that are shampooed no more than once per month. For dogs that swim once per month, flea claims are limited to 5 months and tick claims to 7 months.

f. **MRID 48240119**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 20 domestic short-hair cats were used in the study with 10 each (mixed sex) allocated to either a treatment or control group. 40 ticks were placed on each cat two days prior to placement of collars. 100 fleas were placed on the day before treatment. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 237 days (8 months). Mortality was calculated using Abbott's formula.
(3) Tick efficacy for all exposures exceeded 90% through 239 days after initial placement of the collar (8 months), except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the cats' hair initially). Flea efficacy exceeded 90%

through 239 days after initial placement. Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Ticks, and Fleas.
(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For fleas, the study is acceptable to 8 month control claims on cats.

g. **MRID 48240120**

(1) GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* and *Rhipicephalus sanguineus* ticks and *Ctenocephalides felis* fleas on dogs treated with the collar. Dogs were acclimated and pre-qualified for flea retention. 20 dogs were used in the study with 10 each allocated to either a treatment or control group. 40-50 ticks of each species and 100 fleas were placed on each dog two days prior to placement of collars. All dogs were over 18 lbs. and thus, all dogs received the large collar. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the dogs, with counts and removal at 48 hours. The study was carried through 237 days (8 months). For female ticks, engorgement was determined for female ticks. Mortality was calculated using Abbott's formula. To evaluate repellency, ticks attached to the dogs on day -8 (pre-qualifying) were counted at 3 and 6 hours after placement to verify the appropriateness of time points for evaluation. Tick counts for repellency determination was done the same way after every re-infestation without removal of ticks. A flea larvicidal assessment was conducted on days -7 to -5, and then in 2 to 5 week intervals from day 12 forward to when dogs were not infested with parasites. Fleece-lined board were placed on the floors of dog kennels for 3 hours on 3 consecutive days. Samples were cut from the blankets, placed in petri dishes, and frozen. Remaining parts of the blanket were also frozen and stored. The wooden board was cleaned and a new blanket fixed. After removal from the freezer, petri dishes were allowed to reach room temperature and ~50 flea eggs from the same colony were placed in the middle of the blanket sample. Flea rearing medium was spread over the surface and samples were incubated for 28 days.
(3) Tick efficacy for both species exceeded 90% through 238 days after initial placement, except for the 2 day assessment, which was inadequate (likely due to the time taken for the material to spread through the dogs hair initially). Tick repellency, within hours of placement, for both species exceeded 90% from 27 to 236 days after initial treatment. Adult flea efficacy exceeded 99% from day 2 to day 238 after treatment. Larvicidal effects against fleas exceeded 99% for days 12-245 after treatment. The primary reviewer concurred that the study was adequate to support 8 month flea and tick claims.
(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For *R. sanguineus* and fleas, the study is acceptable to 8 month control claims against ticks and fleas.

h. **MRID 48240121**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate killing efficacy of the test product against *Ixodes ricinus* adult ticks and *Ctenocephalides felis* fleas on cats treated with the collar. Cats were acclimated and pre-qualified for flea retention. 20 domestic short-hair cats were used in the study with 10 each (mixed sex) allocated to either a treatment or control group. 40 ticks were placed on each cat two days prior to placement of collars. 100 fleas were placed on the day before treatment. Ticks and fleas were counted 2 days after placement of collars via removal. Periodic re-infestations were made onto the cats, (alternating between fleas and ticks over the course of the study) with counts and removal at 48 hours. The study was carried through 237 days (8 months). Mortality was calculated using Abbott's formula. To evaluate repellency, ticks attached to the cats on day -8 (pre-qualifying) were counted at 3 and 6 hours after placement to verify the appropriateness of time points for evaluation. Tick counts for repellency determination was done the same way after every re-infestation without removal of ticks. A flea larvicidal assessment was

conducted on days -7 to -5, and then in 2 to 5 week intervals from day 12 forward to when cats were not infested with parasites. Fleece-lined board were placed on the floors of cat transport boxes for 3 hours on 3 consecutive days. Samples were cut from the blankets, placed in petri dishes, and frozen. Remaining parts of the blanket were also frozen and stored. The wooden board was cleaned and a new blanket fixed. After removal from the freezer, petri dishes were allowed to reach room temperature and ~50 flea eggs from the same colony were placed in the middle of the blanket sample. Flea rearing medium was spread over the surface and samples were incubated for 28 days. Efficacy against flea eggs was evaluated by rearing flea eggs with debris that fell out of the cats' hair (100 mg of debris : 100 mg of flea medium). Eggs were incubated for 4 days and hatch was evaluated.
(3) Tick efficacy for all exposures exceeded 90% through 239 days after initial placement of the collar (8 months), for both killing and repellence (237 days). Flea efficacy exceeded 90% through 169 days after initial placement. Larvicidal efficacy exceeded 90% through 37 days. Ovicidal efficacy never reached 90% for flea eggs. Authors conclude that efficacy is supported for fleas and ticks. The primary reviewer concurred that the data was adequate to support 8 month efficacy claims for Ticks. For fleas, the supported efficacy duration was shorter. The author concurred that use of the collar could aid in the control of flea larvae, and thus other fleas in the pets environment.
(4) Because *Ixodes ricinus* is a species known to have similar susceptibility to *Ixodes scapularis* the data are adequate to support 8 month efficacy claims for *Ixodes* ticks. For fleas, the study is acceptable to support a 5 month claim on flea adults, and an aids in control claim for flea larvae. No larvicidal claims are supported.

i. **MRID 48240122**

(1) non-GLP study
(2) A clinical field study was conducted using parasite infested animals. The study enrolled 346 animals from France, Germany, Hungary, and Portugal.
(3) The study is rated supplemental regarding claims on the label for pests found in the United States.

j. **MRID 48240123**

(1) non-GLP study
(2) A clinical field study was conducted using parasite infested animals. The study enrolled 346 animals from France, Germany, Hungary, and Portugal.
(3) The study is rated supplemental regarding claims on the label for pests found in the United States.

k. **MRID 48240124**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of efficacy against cat fleas, *Ctenocephalides felis* on cats. Cats were acclimated and pre-qualified for flea retention. 16 domestic short-hair cats were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. After qualification, 100 fleas were placed on each cat on the day of placement of collars. Fleas were counted 1 day after placement of collars via removal. Mortality was calculated using Abbott's formula.
(3) Flea efficacy at one day after placement (and treatment) was 99.8%. The study authors indicate the study is acceptable to support a claim that the product controls fleas within 24 hours. The primary reviewer concurs with this conclusion.
(4) The study is acceptable to support claims against fleas on cats for killing within 24 hours.

l. **MRID 48240125**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of efficacy against cat fleas, *Ctenocephalides felis* on dogs. Dogs were acclimated and pre-qualified for flea retention. 16 dogs

were used in the study with 8 each (mixed sex) allocated to either a treatment or control group. After qualification, 100 fleas were placed on each cat on the day of placement of collars. Fleas were counted 1 day after placement of collars via removal. Mortality was calculated using Abbott's formula.
(3) Flea efficacy at one day after placement (and treatment) was 100.0%. The study authors indicate the study is acceptable to support a claim that the product controls fleas within 24 hours. The primary reviewer concurs with this conclusion.
(4) The study is acceptable to support claims against fleas on dogs for killing within 24 hours.

m. **MRID 48240126**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of flumethrin against 2 *Ixodes* species in an in vitro exposure assay. Flumethrin was dissolved in acetone and transferred into snap cap vials and centrifuged for 2 hours at room temperature. Vials were uncapped and acetone was evaported to leave a uniform coating on the inside of the vial (44.7 sq cm). Five unfed ticks were transferred to each vial, capped, and kept at room temperature. Efficacy was evaluated by placing vials to a heating table to observe ticks for heat avoidance behavior, after 24 and 48 h exposure. There were 7 dosages tested along with untreated and solvent control groups. There were 6 reps per concentration per tick species, with 5 ticks per vial. Inferential statistical analysis was performed using repeated measures ANOVA with concentration, tick species, and time as fixed effects in the model. The 2 and 3 way interactions were also included as mixed effects into the model.
(3) 24 hour tick efficacy for all species exceeded 90% at doses of 0.288 ppm and higher. For 48 hours, >90% efficacy was observed at doests of 0.0576 ppm and higher. Study authors say these data suggest similar susceptibility responses of the 2 *Ixodes* spp. toward flumethrin.
(4) The study is rated as supplemental, as the data are based upon technical grade active ingredient, and other product specific collar data have already been submitted to support tick efficacy claims. However, the data are acceptable to demonstrate that efficacy data between the two *Ixodes* species are similar and could be used to support bridging arguments for *Ixodes* efficacy data between the two species.

n. **MRID 48240127**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of activity of the submitted collar against *Ixodes ricinus* on cats. 16 cats were assigned to either a treated or control group (8 cats per group). Cats were prequalified for tick retention. Cats were infested with 20 adult female and 15 adult male ticks on SD -6, 0, and 2 (cats were sedated). On SD 2, female ticks were counted and removed at 48 hours after treatment. After re-infestation, tick counts for repellency were made at 6 h after re-infestation. After tick removal, engorgement status was determined. For determination of repellency, the female ticks were specified during counting as dead or alive. Efficacy (mortality or repellency) was calculated using Abbott's formula, and compared statistically between the 2 groups using a 2 tailed Wilcoxon-Mann-Whitney-U-test ($p = 0.05$).
(3) Killing efficacy for ticks at 48 hours after treatment was 95.5%. Repelling efficacy at 6 hours after the SD 2 re-infestation was 100%.
(4) The study is acceptable to support killing claims against *Ixodes* ticks on cats within 48 hours and supports the claims of preventing tick infestations within 48 hours after initial application on cats.

o. **MRID 48240128**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate efficacy against *Ixodes ricinus* ticks on dogs. 14 dogs (7 per treatment) were used in the study, and were housed in individual pens with petroleum jelly barriers to prevent escape of ticks. On SD -2, 40 ticks were placed on each dog. On SD 0, the dogs assigned to the collar group were fitted. Reinfestations were made on days 7, 28, 56, 84,

112, 133, 168, 196, 223, and 238 with 35 ticks placed on each dog. Ticks were counted at 48 h after each infestation. On SD 0, live attached ticks were counted without removal. Efficacy was calculated using Abbott's Formula.
(3) Killing control efficacy for day 2 wasy 89.9, and was 100% for all other reinfestations through day 240.
(4) The study is acceptable to support claims against *Ixodes ricinus* for 8 months.

p. **MRID 48240129**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the onset of activity of the submitted collar against *Ixodes ricinus* and *Rhipicephalus sanguineus* on dogs. 16 dogs were assigned to either a treated or control group (8 dogs per group). Dogs were prequalified for tick retention. Dogs were infested with 20 adult female and 15 adult male *Ixodes* ticks and 50 mixed sex *Rhipicephalus* ticks on SD -5, 0, and 2 (cats were sedated). On SD 2, female *Ixodes* ticks and all *Rhipicephalus* were counted and removed at 48 hours after treatment. After re-infestation, tick counts for repellency were made at 6 h after re-infestation. After tick removal, engorgement status was determined. For determination of repellency, the female ticks were specified during counting as dead or alive. Efficacy (mortality or repellency) was calculated using Abbott's formula, and compared statistically between the 2 groups using a 2 tailed Wilcoxon-Mann-Whitney-U-test ($p = 0.05$).
(3) Killing efficacy for ticks at 48 hours after treatment was 96.8% for *R. sanguineus* and 96.2% for *Ixodes*. Repelling efficacy at 6 hours after the SD 2 re-infestation was 99.2% for *R. sanguineus* and 100% for *Ixodes*.
(4) The study is acceptable to support killing claims against *Ixodes* and *R. sanguineus* ticks on dogs within 48 hours and supports the claims of preventing tick infestations within 48 hours after initial application on dogs.

q. **MRID 48240130**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of flumethrin/imidacloprid against 3 tick species (*Ixodes ricinus*, *Rhipicephalus sanguineus*, and *Dermacentor reticulatus*) in an in vitro exposure assay. An appropriate amount of the test compound mixture (1:1.85 flumethrin: imidacloprid) was dissolved in acetone and transferred into snap cap vials and centrifuged for 2 hours at room temperature. Vials were uncapped and acetone was evaported to leave a uniform coating on the inside of the vial (44.7 sq cm). Five unfed adult ticks, 10 unfed nymphs, or approximately 25 unfed larvae were transferred to each vial, capped, and kept at room temperature. Efficacy was evaluated by placing vials to a heating table to observe ticks for heat avoidance behavior, after 24 and 48 h exposure. There were 8 dosages tested along with untreated and solvent control groups. There was one repolicate per treatment per tick species. Inferential statistical analysis was performed using repeated measures ANOVA with concentration, tick species, and time as fixed effects in the model. The 2 and 3 way interactions were also included as mixed effects into the model.
(3) 24 and 48 hour efficacy for all stages of *Ixodes ricinus* ticks was >90% for concentrations of 7.2 ppm and higher of test material. 24 and 48 hour efficacy for all stages of *Rhipicephales sanguineus* was >90% for concentrations of 1.44 ppm and higher. 24 and 48 hour efficacy for all stages of *Dermacentor reticulatus* ticks was >90% for concentrations of 0.288 ppm and higher.
(4) The study is rated as supplemental, as the data are based upon technical grade active ingredients, and other product specific collar data have already been submitted to support tick efficacy claims.

r. **MRID 48240131**

(1) non-GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of a pet collar against existing natural infestations of dog lice, *Trichodectes canis*. 18 dogs were evaluated in the study, with 9 dogs placed in either a control or treated group. Natural lice infestations were evaluated by

counts at 8 specified sites on each dog and lice were not removed. On SD's -5, -2, -1, 2, 7, 14, 21, 28, and 35, lice counts were made for each dog for a minimum of 5 minutes per dog. Counts at a number of sites were determined based upon finding lice at sites specified in the study. Effectiveness was calculated using Abbott's formula, based upon pre and post-treatment counts for each dog at each interval. Infestation was defined as a dog having at least one louse and viable eggs present or >/= 10 live lice. The effectiveness threshold was set at 95%. Lice counts were also compared statistically using ANOVA.
(3) 48 hour efficacy was 95.1% and efficacy was 100% for the remainder of the study.
(4) The study is acceptable to support claims against dog lice (*Trichodectes canis*) for one month on dogs. Claims longer than one month are not supported by this data set.

s. **MRID 48240132**

(1) GLP study
(2) A laboratory study was conducted to evaluate the killing efficacy of a pet collar against existing natural infestations of sarcoptic mange mites, *Sarcoptes scabiei*. 10 dogs were evaluated in the study, and were determined to be infested with *S. scabiei* but not *Demodex spp.* There was no control group. Dogs were subject to mite counts via skin scrapings on days -2, 29, 60, and 90 from 5 different body areas suspected of being infested. Scrapes were made with a blade to that capillary oozing occurred. The scraping was transferred to a marked microscope slide containing mineral oil for examination for the presence of live mites. Clinical signs and extent of scabietic lesions on each dog were assessed on the days when scrapings were made, and classified via a qualitative scale for scales, and hair loss. Photographs were taken to assist in these qualitative assessments. An overall success rate was calculated by dividing the number of dogs with no live mites by the total number of dogs in the group and multiplying by 100. The study authors defined effectiveness as a success rate that was >/= 90%.
(3) Mite presence was reduced to 10% on days 29 and 60, with 0% mite occurrence by day 90. The percent of dogs showing papules on skin decreased from 75% to 20% by day 90, and skin crusting was reduced similarly. Study authors conclude that since mite numbers were reduced by 100% over the course of the study (along with the other clinical measurements), that the study should support claims against sarcoptic mange mites.
(4) The primary reviewer points out that the lack of a control group is a deficiency, but that overall evidence of mite reduction is acceptable given the design of the study. The study is partially acceptable, and can be used to support an "aids in control" or "aids in treatment" claim for Sarcoptic mange.

t. **MRID 48240133**

(1) non-GLP study
(2) An *in vitro* laboratory study was conducted to evaluate the killing efficacy (speed of kill) for hair clipped from animals treated with a a pet collar--against brown dog tick, *Rhipicephalus sanguineus*. 2 predecessor studies were conducted where hair was clipped from treated animals from various parts of the animal's bodies. For this study, a chest hair sample was taken with a flumethrin content that was most equivalent to the mean group was chosen for a contact test to evaluate the onset of efficacy. Approximately 0.1g of each sample of the left and right chest were taken, weighed, and mixed; for both cats and dogs. 6 unfed adult ticks were counted into glass vials on SD -3 and kept in an incubator. On SD 0, the ticks were placed onto treated hair samples in petri dishes and kept in an incubator. Tick status was evaluated at 2, 6, 8, 12, 24, and 48 h after initial contact. The study was repeated at 7, 14, 21, 30, 59, 90, 120, 149, 181, 210, and 240 days after initial animal treatment with the collar. Status was assessed by visual examination of the ticks reaction to a heating plate. Mortality was assessed and %Efficacy was calculated using Abbott's formula.
(3) For dogs, all ticks were alive at the 2 h examination for every treatment duration. Efficacy reached 100% by the 6 hour examination for all treatment intervals through 210 days. At 240 days, the efficacy did not exceed 90% until 12 hours of exposure had elapsed, but 83% efficacy was observed from 6-8h. For cats, all ticks were alive at the 2 h examination for every treatment

duration. Efficacy reached 100% by the 6 hour examination for all treatment intervals through 210 days. At 240 days, the efficacy did not exceed 90% until 8 hours of exposure had elapsed, but 50% efficacy was observed at 6h. The study author argues that taking atactic ticks would not be able to attach to skin, overall efficacy in dog and cat hair exceeds 98% after 6 h exposure.
(4) The primary reviewer points out that the lack of a control group is a deficiency, as efficacy was based upon comparisons with SD -1 data. The data supports the addition of *R. sanguineus* claims for dogs within 6 hours after initial efficacy has been obtained, and re-infesting ticks are controlled as quickly as 6 hours. Claims against ticks are supported for cats, but not for the 6 hour onset of activity.

u. **MRID 48240134**

This study contains data in support of an imidacloprid spot-on product that is not applicable to this submission. It is rated as supplemental.

v. **MRID 48240137**

This study contains data in support of an imidacloprid spot-on product that is not applicable to this submission. It is rated as supplemental.

IV. RECOMMENDATIONS:

(1) Labeling:

(a) What pests and site/pest combinations may be added as follows to the label based on the submitted or cited data?

For 8 month prevention and treatment of ticks, fleas, on dogs and cats.
For 1 month prevention and treatment of lice on dogs
Kills ticks within 48 hours of treatment or re-infestation
Kills fleas within 24 hours of treatment or re-infestation
Aids in control of flea larvae in pet's environment
Kills lice on dogs
Kills ticks within 6 hours of reinfestation on dogs
Kills re-infesting fleas (after initial 7 days) within 2 hours

(b) What pests and site/pest combinations must be removed from the label?

Claims against lice must not exceed 1 month
Waterproof claims must be clarified as followed:
-In order to maintain an 8 month control duration, dogs must not be bathed more than once per month
-If dogs swim once per month, the control duration must be revised to 5 months
-Water exposure (i.e. immersion, bathing, or prolonged exposure to rain) can only be once per month
Tick claims for killing within 6 hours of reinfestation on cats must be removed—the claim only is supported for dogs.

(c) List changes to the directions for use:

Remove the directions for killing roaches and ants ('in the environment') on page 2.

(d) List changes to the optional marketing claims:

Claims against lice must be limited to one month
All claims related to '8 months' must be limited to fleas and ticks only. Other pests are not controlled for that

duration.

All claims related to control of flea larvae in the pet's environment must be removed or revised to 'aids on control' for fleas in the pet's environment. This product does not provide efficacy as an area-wide/premise treatment against flea larvae.

All disease claims must be deleted, unless the claim is stated "kills/controls xxx pest that may vector yyy."

All claims of "breaking the flea life cycle" must be deleted. This claim implies efficacy against flea eggs and larvae similar to IGR products that are specifically designed to break the flea life cycle for months. This product does not have that level of efficacy against eggs and larvae.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

February 1, 2012

MEMORANDUM: Acute Toxicity Study and Waiver Request DERs for 11556-RLL

Subject:	Name of Pesticide Product:	PNR1427 INSECTICIDE COLLAR
	EPA Reg. No. /File Symbol:	11556-RLL
	DP Barcode:	DP 385538
	Decision No.:	440307
	Action Code:	R110.0
	PC Codes:	129099 (Imidacloprid
		036007 (Flumethrin: 96.2%)

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505P)

Byron T. Backus Feb. 1, 2012

E. McAlister Feb. 1, 2012

To: BeWanda Alexander/Richard Gebken RM 10
Insecticide Branch
Registration Division (7505P)

Registrant: BAYER HEALTHCARE LLC

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
036007 Flumethrin*	4.5%
129099 Imidacloprid	10.0%
Other Ingredient(s):	85.5%
TOTAL	100.0%

*Trans Z-1/trans Z-2 ratio: max 66% trans Z-1 and min 34% trans Z-2

ACTION REQUESTED: The Risk Manager requests:

"Please review attached acute toxicity studies submitted in support of a new end use product containing two active ingredients: one currently registered (imidacloprid) and a new active ingredient (flumethrin)."

BACKGROUND:

The material received for review includes waiver requests for acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, and primary eye irritation (MRIDs 48240102 through 48240105), as well as a primary dermal irritation study (in MRID 48240106) and a dermal sensitization study (MRID 48240107). This product is a collar (PNR1427 Insecticide, with an ingredient statement indicating that it contains 4.5% flumethrin and 10.0% imidacloprid); both ingredients are embedded in a plastic matrix.

COMMENTS AND RECOMMENDATIONS:

1. It is noted by TRB that although Imidacloprid-containing formulations have been registered as cat and dog spot-ons, no Imidacloprid-containing collars have been registered, so this collar represents both a new use for Imidacloprid and a new active ingredient in Flumethrin.

2. A contractor (Summitec Corporation) did the primary reviews on the waiver requests and acute toxicity studies, producing a DER for each; TRB did secondary reviews on the DERs, making revisions where appropriate.

3. TRB concludes that, based on the nature of this product (a plastic collar for use on dogs and/or cats) and the relatively low release rates of the two active ingredients from the collar matrix, waivers are appropriate for the oral toxicity, dermal toxicity, inhalation toxicity and eye irritation studies. The remaining two reports (primary dermal irritation study in MRID 48240106 and dermal sensitization study in 48240107) have been classified as acceptable.

4. The following is the acute toxicity profile for EPA File Symbol 11556-RLL (PNR1427 INSECTICIDE COLLAR), based on the considerations indicated above:

Acute oral toxicity	IV	Waived	MRID 48240102
Acute dermal toxicity	IV	Waived	MRID 48240103
Acute inhalation toxicity	IV	Waived	MRID 48240104
Primary eye irritation	IV	Waived	MRID 48240105
Primary dermal irritation	IV	Acceptable	MRID 48240106
Dermal sensitization	Not a sensitizer	Acceptable	MRID 48240107

5. Based on the acute toxicity profile above, and taking into consideration the proposed uses specified on the label, information in the CSF, and declaration of ingredients on the proposed label, the following would be the precautionary and first aid labeling for EPA File Symbol 11556-RLL as obtained from the Label Review System:

PRODUCT ID #: **011556-00155**

PRODUCT NAME: **PNR1427 INSECTICIDE**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **CAUTION**

Hazards to Humans:

[The registrant has proposed the following: "Do not open package until ready to use. Do not allow children to play with the collar [or reflectors]. Avoid contact with eyes, skin or clothing. Wash thoroughly with soap and cold water after fitting the collar. People with sensitivity reactions to the ingredients of the collar should avoid contact with the collar. [Choking hazard. Contains small parts]. Do not place collar [or reflectors] in mouth. Not intended for use on humans." These statements are acceptable.]

Hazards to Domestic Animals:

[The statements proposed by the registrant are acceptable (refer to http://www.epa.gov/PR_Notices/pr96-6.html). It is noted that the minimum ages (not to be used on puppies under seven weeks of age or kittens under ten weeks of age) are supported by the puppy and kitten studies in MRIDs 48240110 and 48240111, respectively (refer to the TRB review for 11556-155 dated January 27, 2012).

First Aid:

[No statements required; registrant has the option of using Toxicity Category III statements].

6. The CSF (dated 8/25/2010) for EPA File Symbol 11556-RLL should also be reviewed and accepted by the TRB Chemistry Team.

DATA EVALUATION RECORD

CYCLOPROPANECARBOXYLIC ACID
[PNR 1427]

STUDY TYPE: ACUTE ORAL TOXICITY - RAT [OPPTS 870.1100; OECD 425]
ACUTE DERMAL TOXICITY - RAT [OPPTS 870.1200; OECD 402]
ACUTE INHALATION TOXICITY - RAT [OPPTS 870.1300; OECD 403]
ACUTE EYE IRRITATION - RABBIT [OPPTS 870.2400; OECD 405]
ACUTE DERMAL IRRITATION - RABBIT [OPPTS 870.2500; OECD 404]
DERMAL SENSITIZATION - GUINEA PIG [OPPTS 870.2600; OECD 406]
MRID: 48240102, 48240103, 48240104, 48240105, 48240106, and 48240107

Prepared for
Registration Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Summitec Corporation
9724 Kingston Pike, Suite 602
Knoxville, Tennessee 37922

Task Order No. 3-B-37

Primary Reviewer:
Donna L. Fefee, D.V.M.

Signature: Donna L Fefee EZ
Date: JUL 15 2011

Secondary Reviewers:
Thomas C. Marshall, Ph.D., D.A.B.T.

Signature: Thomas C Marshall EZ
Date: JUL 15 2011

Robert H. Ross, M.S., Program Manager

Signature: Robert H. Ross
Date: JUL 15 2011

Quality Assurance:
Jennifer Goldberg, B.S.

Signature: Jennifer Goldberg
Date: JUL 15 2011

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** January 31, 2012
Risk Manager (EPA): 10

STUDY TYPE: Acute Oral Toxicity - Rat; OPPTS 870.1100; OECD 425

TEST MATERIAL: PNR1427 Insecticide (Imidacloprid [10% w/w] + Flumethrin [4.5% w/w]); solid collar.

CITATION: Chopade, H. (2010) Request for waiver from the requirement of acute oral toxicity study - PNR1427 Insecticide. Study Number 33854. Unpublished study prepared by Bayer Healthcare LLC, Animal Health Division, Shawnee Mission, Kansas. August 31, 2010. MRID 48240102.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee Mission, Kansas

EXECUTIVE SUMMARY: Bayer Healthcare LLC, Animal Health Division requests a waiver from the requirement for an acute oral toxicity study (OPPTS 870.1100; OECD 425). The request is based on the following:

The formulation is a solid that contains highly hydrophobic inert ingredients along with active ingredients that have low water solubilities. The study author states that it is therefore impractical to obtain a solution or suspension of the formulation in water, corn oil, or other vehicles commonly used for dosing solids in an acute toxicity study.

According to the study author, U.S. EPA representatives (B. Backus and B. Alexander) considered this waiver request to be reasonable but requested that Bayer Healthcare LLC, Animal Health Division include information on the release rate of the active ingredients from the collar in the justification for the waiver.

Release rates of active ingredients are given in the following representative Companion Animal Safety Studies:

MRIDs 4824018 + 48674702 (61-day study with adult cats; refer to DP 385560 + DP 396978): One collar group: 347.82 mg Imidacloprid and 98.72 mg Flumethrin (equals dosage rates of 89.93 mg Imidacloprid/kg and 25.15 mg Flumethrin/kg or 1.474 mg Imidacloprid/kg/day and 0.412 mg Flumethrin/kg/day).

MRIDs 48240109 + 48674701 (61-day study with adult cats; refer to DP 385560 + DP 396978): One collar group: 971.79 mg Imidacloprid and 224.93 mg Flumethrin (equals dosage rates of 83.42 Imidacloprid/kg and 19.09 mg Flumethrin/kg or 1.368 mg Imidacloprid/kg/day and 0.313 mg Flumethrin/kg/day).

MRID 48240110 (180-day study with puppies; collars were replaced on days 29, 90, 125, and 148; refer to DP 385560 + DP 396978): One collar group: 219.14 mg Imidacloprid and 51.74 mg Flumethrin in the period from Days 0 to 29 (equals dosage rates of 76.98 mg Imidacloprid and 18.69 mg Flumethrin/kg or 2.654 mg Imidacloprid/kg/day and 0.644 mg Flumethrin/kg/day).

MRID 48240111 (180-day study with kittens; collars were replaced on days 29, 90, 125 and 149; refer to DP 385560 + DP 396978): One collar group: 182.81 mg Imidacloprid and 12.69 mg Flumethrin in the period from Days 0 to 29 (equals dosage rates of 123.42 mg Imidacloprid/kg and 8.51 mg Flumethrin/kg or 4.256 mg Imidacloprid/kg/day and 0.293 mg Flumethrin/kg/day).

The label for PNR1427 Insecticide indicates the Flumethrin Trans Z-1/trans Z-2 ratio: max 66% trans Z-1 and min 34% trans Z-2. From MEID 48240203 the rat oral LD50 value for Flumethrin technical (59.9% trans-Z1-isomer and 40.1% trans-Z2- isomer) is 175 mg/kg (1/3 rats dosed at this level died) with a 95% P.L. confidence limit of 42.89 to 104 mg/kg. The dosage rates given above range from 0.293 to 0.644 mg Flumethrin/kg/day; the 0.644 mg corresponds to a cumulative dosage of 18.69 mg/kg given over a 29-day period, or 10.7% of the 175 mg/kg for a single dose LD50.

The LD50 for technical (75%) Imidacloprid is 424 mg/kg for male rats and 450-475 mg/kg for females (refer to MRID 42055331, TXR 0011070). The maximum cumulative dosage in the 61-day studies was 89.93 mg Imidacloprid/kg, or 21.2% of the 424 mg/kg for a single dose LD50.

The following is from a TRB review dated December 29, 2011 for 11556-RLL (DP 392118; TXR 5013553):

The dosage rates from a ~10 g cat collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (28-91 day) Cat & Kitten Studies: Imidacloprid: Mean dosage rate = 1.88 mg/kg/day (range: 0.71-3.72 mg/kg/day). Flumethrin: Mean dosage rate = 0.19 mg/kg/day (range: 0.05-0.44 mg/kg/day).

Long-term (238-245 day) Cat Studies: Imidacloprid: Mean dosage rate = 0.46 mg/kg/day (range: 0.33-0.60 mg/kg/day). Flumethrin: Mean dosage rate = 0.088 mg/kg/day (range: 0.06-0.12 mg/kg/day).

The dosage rates from a ~35 g dog collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (23-91 day) Dog & Puppy Studies: Imidacloprid: Mean dosage rate = 1.49 mg/kg/day (range: 0.70-2.44 mg/kg/day). Flumethrin: Mean dosage rate = 0.24 mg/kg/day (range: 0.07-0.42 mg/kg/day).

Long-term (238-245 day) Dog Studies: Imidacloprid: Mean dosage rate = 0.42 mg/kg/day (range: 0.33-0.52 mg/kg/day). Flumethrin: Mean dosage rate = 0.12 mg/kg/day (range: 0.09-0.18 mg/kg/day).

Based on the relatively low rates of release of these actives (and particularly the very slow release of flumethrin), TRB concludes that the acute oral LD50 toxicity study for this collar can be waived, and that it can be assigned to EPA Toxicity Category IV by this exposure route.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** January 31, 2012
Risk Manager (EPA): 10

STUDY TYPE: Acute Dermal Toxicity - Rat; OPPTS 870.1200; OECD 402

TEST MATERIAL: PNR1427 Insecticide (Imidacloprid [10% w/w] + Flumethrin [4.5% w/w]); solid collar.

CITATION: Chopade, H. (2010) Request for waiver from the requirement of acute dermal toxicity. Study Number 33855. Unpublished study prepared by Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, Kansas. August 31, 2010. MRID 48240103.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee Mission, Kansas

EXECUTIVE SUMMARY: Bayer Healthcare LLC, Animal Health Division requests a waiver from the requirement for an acute dermal toxicity study (OPPTS 870.1200; OECD 402). The request is based on the following:

The formulation is a solid that contains highly hydrophobic inert ingredients along with active ingredients that have low water solubilities. This, along with the fact that it is difficult to pulverize the collar into a fine powder, would make it difficult to properly moisten the ground material with a suitable vehicle in order to maintain the contact with the test animals' skin.

The same rate of release arguments for the active ingredients considered in the oral LD50 waiver can also be applied to this situation.

Based on the relatively low rates of release of these actives (and particularly the very slow release of flumethrin), TRB concludes that the acute dermal LD50 toxicity study for this collar can be waived, and that it can be assigned to EPA Toxicity Category IV by this exposure route.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** January 31, 2012
Risk Manager (EPA): 10

STUDY TYPE: Acute Inhalation Toxicity - Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: PNR1427 Insecticide (Imidacloprid [10% w/w] + Flumethrin [4.5% w/w]); solid collar.

CITATION: Chopade, H. (2010) Request for waiver from the requirement of acute inhalation toxicity study - PNR1427 Insecticide. Study Number 33856. Unpublished study prepared by Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, Kansas. August 31, 2010. MRID 48240104.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee Mission, Kansas

EXECUTIVE SUMMARY: Bayer Healthcare LLC, Animal Health Division requests a waiver from the requirement for an acute inhalation toxicity study (OPPTS 870.1300; OECD 403). The request is based on the following:

The end use formulation is a solid plastic that is difficult to pulverize into a fine powder, and it also is not volatile. It was not possible to grind the material finely enough or suspend the material in the air.

The reviewer agrees that non-volatile products that cannot be readily aerosolized (e.g. plastic, viscous liquids, waxes, and resins) and that are not heated or diluted to an inhalable state during use or application are appropriate candidates for an inhalation waiver.

The reviewer recommends that this waiver be granted.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** February 1, 2012
Risk Manager (EPA): 10

STUDY TYPE: Primary Eye Irritation - Rabbit; OPPTS 870.2400; OECD 405

TEST MATERIAL: PNR1427 Insecticide (Imidacloprid [10% w/w] + Flumethrin [4.5% w/w]); solid collar.

CITATION: Chopade, H. (2010) Request for waiver from the requirement of acute eye irritation toxicity study - PNR1427 Insecticide. Unpublished study prepared by Bayer HealthCare LLC, Animal Health Division, Shawnee Mission, Kansas. August 31, 2010. MRID 48240105.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee Mission, Kansas

EXECUTIVE SUMMARY: Bayer Healthcare LLC, Animal Health Division requests a waiver from the requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405). The request is based on the following:

The formulation is a solid that is difficult to pulverize into a fine powder. It also contains highly hydrophobic inert ingredients along with active ingredients that have low water solubilities. These properties would make it difficult to dissolve or suspend the coarsely pulverized material in a suitable vehicle and accurately measure 100 mg or 0.1 mL.

The Agency recommended use of a cryogenic grinding method for one of the TGAI (Flumethrin). The results of this study (from MRID 48240211 the technical Flumethrin remained a powder at low temperature, but reverted to a glassy substance when brought to room temperature; see TRB review TXR 5013525 dated December 6, 2011) indicated that it was impractical to use this methodology to conduct an eye irritation study.

A primary eye irritation study (in MRID 42055334) conducted on technical (75%) Imidacloprid (refer to TXR 0011070) demonstrated it is in EPA Toxicity Category IV by this exposure route.

In addition, this formulation is a plastic collar, and the actives are embedded in and released only slowly from the matrix.

Based on the above considerations, TRB concludes that a waiver for the eye irritation study is appropriate. The formulation (a dog or cat collar) can be assigned to EPA Toxicity Category IV by this exposure route.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** January 30, 2012
Risk Manager (EPA): 10

STUDY TYPE: Primary Dermal Irritation - Rabbit; OPPTS 870.2500; OECD 404

TEST MATERIAL: PNR 1427; 9.96% Imidacloprid, 4.35% Flumethrin; Lot No.: KP05KF6; EPSL Reference No.: 090626-2R; Gray solid collar; pH: not available; expiration date: December 1, 2009; stored at room temperature; found to be stable for the duration of testing.

CITATION: Durando, J. (2009) PNR 1427: primary skin irritation study in rabbits. Study Number 27805. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. September 30, 2009. MRID 48240106.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee, Kansas

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 48240106), two male and one female, young adult, New Zealand albino rabbits were dermally exposed for 4 hours to 1"x1" pieces of PNR 1427 (9.96% Imidacloprid, 4.35% Flumethrin; Lot #KP05KF6) moistened with 0.1 mL of distilled water. The doses were applied to intact, clipped, 6-cm^2 application sites on the trunk and covered by a 4-ply gauze pad secured with semi-occlusive 3-inch Micropore tape wrapped around the trunk. The animals were observed at 30-60 minutes and 24, 48, and 72 hours after patch removal, and any irritation at the dose sites was scored according to Draize. The animals were supplied by Robinson Services Inc., Clemmons, North Carolina; the body weights and exact ages of the animals were not provided.

There were no observations of edema. At 30-60 minutes after patch removal, all treated sites exhibited very slight erythema (score=1). At 24 hours, very slight erythema remained present on one site but had resolved on the other two sites. At 48 and 72 hours, all sites were clear of erythema, edema, and/or other changes to the skin. No abnormal systemic clinical signs were reported.

In this study, the primary Irritation Index (PII) is 0.33, and the formulation is a slight irritant. PNR 1427 is classified as EPA Toxicity Category IV for primary dermal irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary skin irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

INDIVIDUAL SKIN IRRITATION SCORES [ERYTHEMA/EDEMA]

Animal No.	Sex	Hours after patch removal			
		1	24	48	72
3501	M	1/0	0/0	0/0	0/0
3502	M	1/0	0/0	0/0	0/0
3503	F	1/0	1/0	0/0	0/0
Severity of Irritation - Mean Score		1.00/0.00	0.33/0.00	0.00/0.00	0.00/0.00

A. Observations: There were no observations of edema. At 30-60 minutes after patch removal, all treated sites exhibited very slight erythema (score=1). At 24 hours, very slight erythema remained present on one site but had resolved on the other two sites. At 48 and 72 hours, all sites were clear of erythema, edema, and/or other changes to the skin. No abnormal systemic clinical signs were reported.

B. Results: The PDII is 0.33.

C. Reviewer's Conclusions: In agreement with the study author, the test material is a slight irritant. The test material is classified as EPA Toxicity Category IV.

D. Deficiencies: As a minor deficiency, the ages of the animals were not provided.

EPA Reviewer: Byron T. Backus, Ph.D. **Date:** January 30, 2012
Risk Manager (EPA): 10

STUDY TYPE: Dermal Sensitization – Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: PNR 1427; 9.96% Imidacloprid, 4.35% Flumethrin; Lot No.: KP05KF6; EPSL Reference No.: 090626-2R; Gray solid collar; pH: not available; expiration date: December 1, 2009; stored at room temperature; found to be stable for the duration of testing.

CITATION: Durando, J. (2009) PNR 1427: dermal sensitization study in guinea pigs (Buehler method). Study Number 27806. Unpublished study prepared by Eurofins | Product Safety Laboratories, Dayton, New Jersey. October 12, 2009. MRID 48240107.

SPONSOR: Bayer Healthcare LLC, Animal Health Division, 12707 W. 63rd Street, Shawnee, Kansas

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 48240107), twenty young adult, male, Hartley albino guinea pigs were tested with PNR 1427 (9.96% Imidacloprid, 4.35% Flumethrin; Lot #KP05KF6) using the Buehler method. For induction and challenge the test material was applied as a 20-22 mm circle (cut from the solid material), moistened with 0.1 mL of distilled water and held in place with non-allergenic Durapore adhesive tape. A separate naïve control group of ten males was treated during challenge only. The animals were supplied by Elm Hill Breeding Labs, Chelmsford, Massachusetts and weighed 302-400 g; exact ages of the animals were not reported.

No positive dermal reactions were seen following challenge. No abnormal systemic clinical signs were reported, and all of the animals gained weight over the course of the study.

Based on this study, PNR 1427 is *not* a dermal sensitizer.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. PROCEDURE

A. Induction: The dorsal area and flanks of the animals were clipped one day prior to each treatment. For each of three successive weekly inductions, a 20-22 mm circle (cut from the solid test material) moistened with 0.1 mL of distilled water was applied to the left side of each animal and secured in place with adhesive tape wrappings for six hours. Reactions were scored 24 and 48 hours post application.

B. Challenge: Twenty-seven days after the first induction, the test animals were challenged with a 20-22 mm circle (cut from the solid test material) moistened with 0.1 mL of distilled water, applied to naive sites on the right side of each animal for 6 hours using the same procedure as described for induction. Reactions were scored 24 and 48 hours post application.

C. Naive Controls: At challenge, a separate "naive" group of ten previously untreated animals was also treated with a 20-22 mm circle (cut from the solid test material) moistened with 0.1 mL of distilled water. Reactions were scored 24 and 48 hours post application.

II. RESULTS and DISCUSSION:

A. Reactions and duration: No erythema was seen at any dose site, following induction or challenge.

B. Positive control: The study report included the results from a positive control study with alpha-Hexylcinnamaldehyde (EPSL Study #27592, completed on June 26, 2009). The positive control study was conducted within six months of the submitted study, and the study author stated that the induction and challenge procedures used in both studies were similar. The reviewer considers the results to be appropriate.

C. Reviewer's Conclusions: In agreement with the study author, the test material is *not* a dermal sensitizer.

D. Deficiencies: According to minutes taken during a teleconference between representatives of Bayer Healthcare LLC, Animal Health Division and representatives of the U.S. EPA (provided in MRIDs 48240102, 48240103, 48240104, 48240105), a U.S. EPA respresentative requested that a dermal sensitization be conducted using ground collar material. The current study instead used cut pieces of the collar with no explanation provided. As a minor deficiency, the ages of the animals were not provided.

ACUTE TOX ONE-LINERS:

1. **DP BARCODE:** 385538				
2. **PC CODES:** 129099, 036007				
3. **CURRENT DATE:** February 1, 2012				
4. **TEST MATERIAL:** PNR 1427 (9.96% Imidacloprid, 4.35% Flumethrin; Lot #KP05KF6)				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox. Cat.**	**Core Grade**
Acute oral toxicity / rat Bayer HealthCare LLC, Animal Health Division Study #33854 / August 31, 2010	48240102	Waiver Recommended	IV	W
Acute dermal toxicity / rat Bayer HealthCare LLC, Animal Health Division Study #33855 / August 31, 2010	48240103	Waiver Recommended	IV	W
Acute inhalation toxicity / rat Bayer HealthCare LLC, Animal Health Division Study #33856 / August 31, 2010	48240104	Waiver Recommended ·	IV	W
Primary eye irritation / rabbit Bayer HealthCare LLC, Animal Health Division Study #33857 / August 31, 2010	48240105	Waiver Recommended.	IV	W
Primary dermal irritation /rabbit Eurofins | Product Safety Laboratories Study #27805 / September 30, 2009	48240106	Slight irritant; PII=0.33	IV	A
Dermal Sensitization /guinea pig Eurofins | Product Safety Laboratories Study #27806 / October 12, 2009	48240107	*Not* a sensitizer	--	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

December 29, 2011

MEMORANDUM: IMIDACLOPRID 10%/FLUMETHRIN 4.5% DOG & CAT COLLARS: DOSAGE AND RELEASE RATES OF ACTIVES

Subject:	Name of Pesticide Product:	PNRI427 INSECTICIDE
	EPA Reg. No. /File Symbol:	11556-RLL
	DP Barcode:	DP 392118
	Decision No.:	440307
	Action Code:	RI10.0
	PC Code:	036007 (Flumethrin: 4.5%)
		129099 (Imidacloprid: 10.0%)

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505P)

Byron T. Backus
12/29/2011
M Backus, Ph.D.

To: BeWanda Alexander/Richard Gebken RM 10
Insecticide Branch
Registration Division (7505P)

Registrant: BAYER HEALTHCARE LLC

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
036007 Flumethrin	4.5%
129099 Imidacloprid	10.0%
Other Ingredient(s):	85.5%
TOTAL	100.0%

Action Requested: The Risk Manager requests a review of MRID 482401-40, a 117-page document summarizing dosages and release rates of imidacloprid and flumethrin from a number of cat and dog collar studies.

COMMENTS AND RECOMMENDATIONS:

The following is the executive summary for the review compilation in MRID 48240140:

The material in MRID 48240140 represents the compilation of release rates in a series of studies of the two active ingredients from cat and dog collars containing ~10% Imidacloprid and ~4.5% Flumethrin. Collars were weighed, then worn by cats or dogs for varying periods of time, after which they were weighed and analyzed for content of the two active ingredients.

The dosage rates from a ~10 g cat collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (28-91 day) Cat & Kitten Studies: Imidacloprid: Mean dosage rate = 1.88 mg/kg/day (range: 0.71-3.72 mg/kg/day). Flumethrin: Mean dosage rate = 0.19 mg/kg/day (range: 0.05-0.44 mg/kg/day).

Long-term (238-245 day) Cat Studies: Imidacloprid: Mean dosage rate = 0.46 mg/kg/day (range: 0.33-0.60 mg/kg/day). Flumethrin: Mean dosage rate = 0.088 mg/kg/day (range: 0.06-0.12 mg/kg/day).

The dosage rates from a ~35 g dog collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (23-91 day) Dog & Puppy Studies: Imidacloprid: Mean dosage rate = 1.49 mg/kg/day (range: 0.70-2.44 mg/kg/day). Flumethrin: Mean dosage rate = 0.24 mg/kg/day (range: 0.07-0.42 mg/kg/day).

Long-term (238-245 day) Dog Studies: Imidacloprid: Mean dosage rate = 0.42 mg/kg/day (range: 0.33-0.52 mg/kg/day). Flumethrin: Mean dosage rate = 0.12 mg/kg/day (range: 0.09-0.18 mg/kg/day).

This report is classified as acceptable (Non-Guideline). It provides useful information regarding the rates of release of the two active ingredients from a collar containing ~10% Imidacloprid and ~4.5% Flumethrin and the exposure to cats and dogs wearing this collar.

Reviewer: Byron T. Backus, Ph.D. **Date:** December 29, 2011
Risk Manager (EPA): 10

STUDY TYPE: Active Release Rates from Cat & Dog Collars (Non-Guideline)

TEST MATERIAL: Collars containing ~10% Imidacloprid and ~4.5% Flumethrin

CITATION: Stanneck, D. (2010) Dosage of the Imidacloprid 10% Flumethrin 4.5% Collar and Release of the Active Ingredients over Time in Cats and Dogs: Review Compilation. Project Number: 35992, PNR1427. Unpublished study prepared by Bayer HealthCare, LLC. 120 p. June 28, 2010. MRID 48240140.

SPONSOR: Bayer HealthCare, LLC
Animal Health Division
P.O. Box 390
Shawnee Mission, KS 66201-0390

EXECUTIVE SUMMARY:

The material in MRID 48240140 represents the compilation of release rates in a series of studies of the two active ingredients from cat and dog collars containing ~10% Imidacloprid and ~4.5% Flumethrin. Collars were weighed, then worn by cats or dogs for varying periods of time, after which they were weighed and analyzed for content of the two active ingredients.

The dosage rates from a ~10 g cat collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (28-91 day) Cat & Kitten Studies: Imidacloprid: Mean dosage rate = 1.88 mg/kg/day (range: 0.71-3.72 mg/kg/day). Flumethrin: Mean dosage rate = 0.19 mg/kg/day (range: 0.05-0.44 mg/kg/day).

Long-term (238-245 day) Cat Studies: Imidacloprid: Mean dosage rate = 0.46 mg/kg/day (range: 0.33-0.60 mg/kg/day). Flumethrin: Mean dosage rate = 0.088 mg/kg/day (range: 0.06-0.12 mg/kg/day).

The dosage rates from a ~35 g dog collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (23-91 day) Dog & Puppy Studies: Imidacloprid: Mean dosage rate = 1.49 mg/kg/day (range: 0.70-2.44 mg/kg/day). Flumethrin: Mean dosage rate = 0.24 mg/kg/day (range: 0.07-0.42 mg/kg/day).

Long-term (238-245 day) Dog Studies: Imidacloprid: Mean dosage rate = 0.42 mg/kg/day (range: 0.33-0.52 mg/kg/day). Flumethrin: Mean dosage rate = 0.12 mg/kg/day (range: 0.09-0.18 mg/kg/day).

This report is classified as acceptable (Non-Guideline). It provides useful information regarding the rates of release of the two active ingredients from a collar containing ~10% Imidacloprid and ~4.5% Flumethrin and the exposure to cats and dogs wearing this collar.

COMPLIANCE: Signed and dated GLP (noting that this study was not conducted in full compliance with GLP standards), and Data Confidentiality statements were provided. There is no Quality Assurance Statement (presumably because this report represents a review compilation).

RESULTS:

Collars were weighed, then worn by cats or dogs for varying periods of time, after which they were weighed and analyzed for content of the two active ingredients.

Cat studies:

Dosage rates in cat studies (from Table 5 on p. 8 of MRID 48240140):

Study Number	Breed & (body weight range in kg)	Study Duration (Days)	Imidacloprid exposure (mg/kg/day)	Flumethrin exposure (mg/kg/day)
146.266	DSH (3.3-5.1)	2	7.36	0.18
		7	4.73	0.18
		14	3.03	0.23
		28	2.08	0.12
		56	1.44	0.10
		84	1.13	0.18
146.164	DSH (2.3-5.1)	30	3.04	0.44
		238	0.56	0.12
146.303	DSH (3.7-4.7)	238	0.39	0.06
146.159	Mix (2.1-4.7)	60	1.27	0.20
152.152	DSH (2.8-5.3)	61	1.62	0.32
152.150	DSH kittens (0.97-1.26 study day 0)	30	3.72	0.20
		60	1.91	0.14
146.747	DSH (3.6-5.7)	28	0.71	0.05
146.156	DSH (2.8-5.3)	238	0.42	0.07
146.045	DSH (3.8-7.0)	241	0.33	0.10
146.155	DSH (2.7-	240	0.60	0.09

There are two mechanisms by which an active can be released from a collar: 1) Simple wear, and 2) Diffusion from the matrix. An approximation of the amount of an active released from wear can be calculated by: weight loss – (amount of imidacloprid lost + amount of flumethrin loss) = amount of plastic lost. Then: (amount of plastic lost)/[1 – (original percentage of imadocloprid + original percentage of flumethrin)] = total amount lost by wear. Then: (total amount lost by wear) x (original percentage of imadocloprid) = amount of imidacloprid lost by wear , and: (total amount lost by wear) x (original percentage of flumethrin) = amount of flumethrin lost by wear. The table below shows that for the cat collar most of the imidacloprid is released by diffusion (the total amount released by wear is approximately 10-14% for 28 days and about 42% for 240 days), while most of the flumethrin is released by wear (the mean total percentage released by wear in the 5 cat studies below which ran for 238-241 days is 99.46%).

Study Number	Body weight range in kg	Study Duration (Days)	Mean collar weight loss (mg)	Plastic weight loss (mg)	Amount of Imidaclo prid released (mg)	Amount of flumethrin released (mg)	Amount in mg of imidacloprid released by wear and % total	Amount in mg of flumethrin released by wear (% total released)
146.156	3.2-5.4	238	2024.44	1518.97	433.1	72.37	179.64 (41.48)	80.04 (110.6)
146.164	2.56-4.22	30	1198.75	860.75	295.58	42.43	100.67 (34.06)	45.30 (106.8)
	2.28-5.14	240	2160.0	1634.56	435.3	90.14	191.18 (43.92)	86.03 (95.44)
146.159	2.4-4.7	60	907.33	634.99	235.60	36.74	72.61 (30.82)	33.34 (90.75)
146.303	3.7-4.7	238	1798.75	1340.35	394.45	63.95	158.52 (40.19)	70.63 (110.44)
146.747	3.6-5.7	28	458.75	239.71	205.34	13.7	27.38 (13.33)	12.29 (89.73)
146.266	3.5-4.1	2	33.33	N.V.	54.67	1.53	N.C.	N.C.
	3.4-5.1	7	133.33	16.36	109.0	7.97	1.93 (1.77)	0.86 (10.82)
	3.4-5.1	14	266.67	103.57	149.5	13.60	12.25 (8.19)	5.46 (40.13)
	3.4-5.1	28	366.67	160.01	195.53	11.13	18.92 (9.68)	8.43 (75.75)
	3.5-5.1	56	633.33	344.69	266.87	21.77	40.77 (15.28)	18.16 (83.43)
	3.3-3.7	84	1000.00	648.2	312.4	39.40	76.66 (24.54)	34.16 (86.69)
146.045	4.6-6.0	241	2197.0	1656.37	411.21	129.42	195.89 (47.64)	87.28 (67.44)
146.155	2.5-3.6	240	1804.0	1334.52	407.48	62.00	157.83 (38.73)	70.32 (113.42)
146.100	2.38-5.8	226[a]	1502.5[a]	1294.77[a]	177.54[a]	30.19[a]	33.98 (19.14)	30.59 (101.31)
	2.58-3.36	226[b]	1696.25[b]	1315.76[b]	349.89[b]	30.60[b]	70.93 (20.27)	31.92 (104.31
	2.28-4.36	226[c]	1725.0[c]	1402.13[c]	297.44[c]	25.43[c]	159.79 (53.72)	35.95 (141.37)

Data calculated from information (Tables) on p. 36, 37, 38, 39, 40, 41, 42

[a]Collar supposedly contained 2.5% Imidacloprid and 2.25% Flumethrin and this reviewer's calculations above are based on that composition; however, column 6 of the Table on p. 44 of MRID 48240140 indicates the collar contained 10.1% Imidacloprid and column 7 indicates it contained 4.5% Flumethrin.

[b]Collar supposedly contained 5.0% Imidacloprid and 2.25% Flumethrin and this reviewer's calculations above are based on that composition; however, column 6 of the Table on p. 44 of MRID 48240140 indicates the collar contained 10.1% Imidacloprid and column 7 indicates it contained 4.5% Flumethrin.

[c]Collar supposedly contained 10.0% Imidacloprid and 2.25% Flumethrin and this reviewer's calculations above are based on that composition; however, column 6 of the Table on p. 44 of MRID 48240140 indicates the collar contained 10.1% imidacloprid and column 7 indicates it contained 4.5% Flumethrin.

Dog studies:

Dosage rates in dog studies (from Table 6 on p. 8 of MRID 48240140):

Study Number	Breed & (body weight range in kg)	Study Duration (Days)	Imidacloprid exposure (mg/kg/day)	Flumethrin exposure (mg/kg/day)
146.165	Mongrel (11.6-19.4)	30	1.62	0.20
		238	0.33	0.11
146.306	Beagle (9.4-13.6)	238	0.52	0.18
146.161	Mix (8.4-20.2)	60	0.89	0.07
152.151	Beagle (8.7-13.4)	60	1.37	0.15
152.149	Beagle puppies (1.5-2.9 on study day 0)	23	2.44	0.36
		30	2.21	0.42
		60	0.97	0.28
146.737	Beagle (8.7-11.7)	28	2.25	0.20
146.158	Beagle (8.8-12.8)	245	0.52	0.11
146.390	Beagle (6.6-20.4)	240	0.35	0.09
146.592	Beagle (8.3-13.5)	240	0.37	0.13
146.269	Mongrel (7.1-21.5)	90	0.70	0.32
146.607	Beagle (10.0-13.1)	91	0.97	0.18

The table below shows that for the dog collar most of the imidacloprid is released by diffusion (the total amount released by wear is approximately 8-22% for 28-30 days and about 29-61.5%, with a mean of ~44% for 238-245 days), while most of the flumethrin is released by wear (the mean total percentage released by wear in the 5 dog collar studies below which ran for 238-245 days was 64.4%).

Study Number	Body weight range in kg)	Study Duration (Days)	Mean collar weight loss (mg)	Plastic weight loss (mg)	Amount of Imidaclo prid released (mg)	Amount of flumethrin released (mg)	Amount in mg of imidacloprid released from wear and % total	Amount in mg of flumethrin released from wear (% total released)
146.164	(11.6-19.4)	30	2145.7	1342.5	715.74	87.49	155.26 (21.69)	70.57 (80.66)
		240	6921.4	5155.95	1310.19	455.26	596.31 (45.51)	271.05 (59.54)
146.158	(8.8-12.8)	245	5136.0	3481.85	1358.7	295.45	406.76 (29.94)	178.97 (60.58)
146.306	(9.4-13.6)	238	6238.8	4458.65	1321.25	458.9	520.87 (39.42)	229.18 (49.94)
146.362/ 146.607	(10.0-13.1)	91	3498.3	2319.43	998.3	180.57	268.25 (26.87)	104.37 (57.8)
146.737	(9.1-11.0)	28	1142.5	445.99	640.61	55.9	51.58 (8.05)	23.45 (41.95)
146.390	(10.4-18.2)	240	5718.0	4297.67	1126.98	303.35	500.90 (44.45)	220.39 (72.65)
146.269	(7.22-21.48)	90	3696.25#	2621.89	796.3	278.06	303.23 (38.08)	137.83 (49.57)
146.161	(10.36-17.56)	60	1633.75	797.53	797.61	38.61	92.24 (11.56)	41.93 (108.59)
146.592	(8.3-13.5)	240	6467.14	5156.91	969.07	341.16	596.42 (61.5)	271.10 (79.46)

Data calculated from information (Tables) on p. 45, 46, 47, 48, 49, 50, 51, 52, and 53.
#No weight loss reported for collar from one dog (CC0CE2); data from this dog not included in calculations by the EPA reviewer.

For the dog studies that ranged from 238-245 days the mean collar weight loss was 6096.27 (range: 5136.0-6921.4) mg; the mean plastic (matrix) weight loss was 4510.21 (range: 3481.85-5156.91) mg; the mean total amount of imidacloprid released per collar was 1217.24 (range: 969.07-1358.7) mg; and the mean total amount of flumethrin released per collar was 370.82 (range: 295.45-458.9) mg. The approximate amount of imidacloprid released per collar from wear was 524.25 (range: 406.76-596.42) mg and the approximate amount of flumethrin released per collar from wear was 234.14 (range: 178.97-271.1) mg.

The following summarizes the dosages given in Tables 5 and 6 on p. 8 of MRID 48240140:

Short-Term (28-91 day) Cat & Kitten Studies:	Imidacloprid exposure (mg/kg/day): 2.08, 1.44, 1.13, 3.04, 1.27, 1.62, 3.72*, 1.91*, 0.71 **[Mean = 1.88]**	Flumethrin exposure (mg/kg/day): 0.12, 0.10, 0.18, 0.44, 0.20, 0.32, 0.20*, 0.14*, 0.05 **[Mean = 0.19]**
Long-Term (238-245 day) Cat Studies:	Imidacloprid exposure (mg/kg/day): 0.56, 0.39, 0.42, 0.33, 0.60 **[Mean = 0.46]**	Flumethrin exposure (mg/kg/day): 0.12, 0.06, 0.07, 0.10, 0.09 **[Mean = 0.088]**
Short-Term (23-91 day) Dog & Puppy Studies:	Imidacloprid exposure (mg/kg/day): 1.62, 0.89, 1.37, 2.44**, 2.21**, 0.97**, 2.25, 0.70, 0.97 **[Mean = 1.49]**	Flumethrin exposure (mg/kg/day): 0.20, 0.07, 0.15, 0.36**, 0.42**, 0.28**, 0.20, 0.32, 0.18 **[Mean = 0.24]**
Long-Term (238-245 day) Dog Studies:	Imidacloprid exposure (mg/kg/dau): 0.33, 0.52, 0.52, 0.35, 0.37 **[Mean = 0.42]**	Flumethrin exposure (mg/kg/day): 0.11, 0.18, 0.11, 0.09, 0.13 **[Mean = 0.12]**

*Kitten study
**Puppy study

Reviewer's Conclusions:

The dosage rates from a ~10 g cat collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (28-91 day) Cat & Kitten Studies: Imidacloprid: Mean dosage rate = 1.88 mg/kg/day (range: 0.71-3.72 mg/kg/day). Flumethrin: Mean dosage rate = 0.19 mg/kg/day (range: 0.05-0.44 mg/kg/day).

Long-term (238-245 day) Cat Studies: Imidacloprid: Mean dosage rate = 0.46 mg/kg/day (range: 0.33-0.60 mg/kg/day). Flumethrin: Mean dosage rate = 0.088 mg/kg/day (range: 0.06-0.12 mg/kg/day).

The dosage rates from a ~35 g dog collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following:

Short-term (23-91 day) Dog & Puppy Studies: Imidacloprid: Mean dosage rate = 1.49 mg/kg/day (range: 0.70-2.44 mg/kg/day). Flumethrin: Mean dosage rate = 0.24 mg/kg/day (range: 0.07-0.42 mg/kg/day).

Long-term (238-245 day) Dog Studies: Imidacloprid: Mean dosage rate = 0.42 mg/kg/day (range: 0.33-0.52 mg/kg/day). Flumethrin: Mean dosage rate = 0.12 mg/kg/day (range: 0.09-0.18 mg/kg/day).

This report is classified as acceptable (Non-Guideline). It provides useful information regarding the rates of release of the two active ingredients from a collar containing ~10% Imidacloprid and ~4.5% Flumethrin and the exposure to cats and dogs wearing this collar.

ACUTE TOX ONE-LINERS:

1. **DP BARCODE:** 392118				
2. **PC CODES:** 129099 (Imidacloprid); 036007 (Flumethrin)				
3. **CURRENT DATE:** December 29, 2011				
4. **TEST MATERIAL:** Dog & Cat Collars containing ~10% Imidacloprid & ~4.5% Flumethrin				
Study/Species/Lab Study # / Date	**MRID**	**Results**	**Tox. Cat.**	**Core Grade**
Dosages & release rates of actives (review compilation)/cats & dogs/ Bayer Animal Health, Monheim, Germany/PNR 1427/June 28, 2010	48240140	**Short-term (28-91 day) Cat & Kitten Studies:** Imidacloprid: Mean dosage rate = 1.88 mg/kg/day (range: 0.71-3.72 mg/kg/day). Flumethrin: Mean dosage rate = 0.19 mg/kg/day (range: 0.05-0.44 mg/kg/day). **Long-term (238-245 day) Cat Studies:** Imidacloprid: Mean dosage rate = 0.46 mg/kg/day (range: 0.33-0.60 mg/kg/day). Flumethrin: Mean dosage rate = 0.088 mg/kg/day (range: 0.06-0.12 mg/kg/day). The dosage rates from a ~35 g dog collar containing ~10% Imidacloprid and ~4.5% Flumethrin were the following: **Short-term (23-91 day) Dog & Puppy Studies:** Imidacloprid: Mean dosage rate = 1.49 mg/kg/day (range: 0.70-2.44 mg/kg/day). Flumethrin: Mean dosage rate = 0.24 mg/kg/day (range: 0.07-0.42 mg/kg/day). **Long-term (238-245 day) Dog Studies:** Imidacloprid: Mean dosage rate = 0.42 mg/kg/day (range: 0.33-0.52 mg/kg/day). Flumethrin: Mean dosage rate = 0.12 mg/kg/day (range: 0.09-0.18 mg/kg/day).	n/a	A (non-Guideline)

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived

EN . RONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

FEE

DATE OUT: October 11, 2011 ACTION CODE: 570
SUBJECT: STORAGE STABILITY (830.6317) & CORROSION CHARACTERISTICS (830.6320) REVIEW
ACCELERATED STUDY [ ]; ONE YEAR STUDY [X[; OVER I YEAR STUDY [ ]
MP [ ] EP [X] EUP [ ]
DP BARCODE No.: 388440 REG. No. :11556-RLL
DECISION No.: 440307 MRID No(s): 484165-01
PRODUCT NAME: PNR1427 INSECTICIDE
COMPANY: BAYER HEALTHCARD LLC

FROM: William Herald / Microbiologist (MS) / CHEMIST, REHS / Registered Sanitarian
Product Chemistry Team
Technical Review Branch/RD (7505P)

TO: BeWanda Alexander / Richard Gehken, RM 10
Insecticide Branch / RD (7505P)

I. CONCLUSIONS:

STORAGE STABILITY (830.6317):
[X] ACCEPTABLE
[ ] UNACCEPTABLE*
[ ] UPGRADEABLE*

40CFR158.190 DATA REQUIREMENT: [X] SATISFIED [ ] NOT SATISFIED

CORROSION CHRACTERISTICS (830.6320):
[X] ACCEPTABLE
[ ] UNACCEPTABLE*
[ ] UPGRADEABLE*

40CFR158.190 DATA REQUIREMENT: [X] SATISFIED [ ] NOT SATISFIED

* If unacceptable or upgradeable describe the deficiency and provide recommendations

Comments & Recommendations:

II. STUDY SUMMARY

A. STUDY CONDUCTED UNDER US GLP/OECD GUIDELINES

[X] Yes [ ] No

B. PRODUCT INFORMATIO

Active ingredients:

Lahel claims Nominal concentrations (%):

Flumethrin.....	4.5%
Imidacloprid.....	10.0%

Initial concentrations of the AIs (%) used in the study:

Flumethrin.....	4.656% (average)
Imidacloprid.....	10.13% (average)

Lower certified limits (%) based on AI % in the study:

Flumethrin.....	4.422%
Imidacloprid.....	9.62%

C. EXPERIMENTAL PARAMETERS

Temperature: Ambient room temperatures for one year.
Duration of study: [X] 1 year
Types of containers: Plastic bags.
Analysis at intervals: [X] 0 (initial); [X] 3 months; [X] 6 months
[X] 9 months; and [X] 12 months.

D. ANALYTICAL METHOD

Method	DETECTOR
High Pressure Liquid chromatography (HPLC)	UV/VIS (268nm)

E. RESULTS

1) Compared to the initial concentrations of the active ingredients in the study, the report shows that the AIs% remained will within the statutory parameters required in Title 40 CFR § 158.350 during the 3rd, 6th, 9th and 12th month testing periods while stored at ambient room temperatures.

2) The study reported that there was no observed corrosive effect from the test substance; the collar remained a solid gray throughout the study. No corrosive effects during the study were ohserved. There were no corrosion of the packaging was ohserved. All of the packaging remained intact and no leaking or deforming of the package was noticed.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

DP BAR CODE NO.: 385540 **FILE SYMBOL NO.: 11556-RLL** **DECISION NO.: 440307**
PC Code(s): 129099,036007 **ACTION CODE: R110.0**
FOOD Use: No **NON-FOOD Use: Yes**

DATE OUT: October 11, 2011

SUBJECT: End Use Product Chemistry Review
Product Name: PNR 1427 Insecticide

FROM: Hari Mukhoty
Product Chemistry Team
Technical Review Branch / Registration Division (7505P) 10/11/11

TO: BeWanda Alexander / Richard Gebken PM - 10
Insecticide Branch / Registration Division (7505P)

Company Name: Bayer HealthCare LLC
Formulation Type: Solid

INTRODUCTION:

The Registrant has submitted one basic CSF (dated: 08/25/2010), two amended CSFs (Dated: 08/25/2010) as alternate formulations (Alt. # 1 & # 2) to the aforesaid basic and has proposed a product specific label for registration of the aforesaid products under EPA File Symbol No. 11556-RLL.

TRB has been requested to evaluate the product chemistry data required for the registration of the proposed products.

SUMMARY OF FINDINGS:

1. Name of Active Ingredient(s): Imidacloprid (10.0%), Flumethrin (4.50%).

2. Has the registrant claimed substantial similarity to registered product?
[ ] Yes [X] No [ ] NA If yes: EPA Reg. No.

3. The source material(s) of the active ingredient(s) is/are registered with the Agency. The source of the active ingredient Flumethrin is not, as of this date, registered with the Agency. The nominal concentration of this active ingredient (4.50%) has been tentatively calculated based on the claimed purity of the chemical by the registrant to be 96.2%.

4. All inert ingredients have been screened by IIAB on 10/06/2010 and have been found to be approved for non-food uses only.

5. The CSFs of the proposed basic and alternate formulations have been filled out completely and correctly based on the claimed purity of the active ingredient Flumethrin.

DP BAR CODE NO.: 385540 **FILE SYMBOL NO.: 11556-RLL** **DECISION NO.: 440307**
PC Code(s): 129099,036007 **ACTION CODE: R110.0**
FOOD Use: No **NON-FOOD Use: Yes**

6. Confidential Statement of Formula(s):

[X] Basic - Dated: 08/25/2010 re-submitted – Dated: NA

[X] Alternate- # 1 & # 2 Dated: 08/25/2010 re-submitted: Dated: NA

Alternate CSF(s) complies with 40CFR §152.43: [X] Yes [ ] No NA [ ].

7. Product label

a. Ingredient statement: Nominal concentration of AI listed on CSF(s) concur with product label (PR Notice 91-2)
[X] Yes

Is the sub statement in compliance with PR Notice 97-6?

] X] Yes [ ] No - Uses the term "Other Ingredients"
, if not, explain below:

Metallic equivalent:	[ ] Yes [X [NA
Soluble arsenic:	[ ] Yes [X [NA
Isomeric ratios:	[[Yes [X [NA
Acid equivalent:	[ ] Yes [X] NA

b. Health related sub statements:

Petroleum distillate at > 10%: [ ] Yes [ ] No [X [NA
Methanol at > 4%: [ ] Yes [ ] No [X [NA
Sodium Nitrate / Sodium Nitrite [ ]Yes [[No [X] NA

c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for: flammability, explosive potential or electric insulator breakdown?

[ ] Yes] X] No

Total Release Fogger PR Notice 98-6 (40 CFR 156.78 d): [[Yes [ ] No [X] NA

d. Label requires an additional Storage and Disposal statement: [ ] Yes [X] No – from product chemistry point of view; if yes explain below:

Final decision of overall label acceptance will be made by the PM.

DP BAR CODE NO.: 385540 **FILE SYMBOL NO.: 11556-RLL** **DECISION NO.: 440307**
PC Code(s): 129099,036007 **ACTION CODE: R110.0**
FOOD Use: No **NON-FOOD Use: Yes**

8. Group A: Product Chemistry Data

TRB's determination of the acceptability of the data for the proposed product is listed in the tables below.

Guideline No.	Study Title		Data submitted		TRB's Assessment of Data	MRID Nos. 482401-01
			Yes	No		
830.1550	Product Identity & Composition		X		A	"
830.1600	Description of materials used to produce the product		X		A	"
830.1650	Description of formulation process		X		A	"
830.1670	Discussion on the formation of impurities		X		A	"
830.1750	Certified limits (158.350)	Standard certified Limits	X		A	"
		Proposed limits			N/A	
830.1800	Enforcement Analytical Method #		X		A	"

A = Acceptance, NA = Not Acceptable, G = Data Gap,
W = Waiver Request, I = In Progress, N/A = Not Applicable
# = HPLC using UV detector set at 268 nm

9. Group **B:**

Guideline No.	Study Title	Value or Qualitative Description	TRB's Assessment of Data	MRID Nos. 482401-01
830.6303	Physical State	Solid	A	"
830.6315	Flammability	Product is solid	A	"
830.6316	Explodability	Product does not contain any explosive ingredient	A	"
830.7000	pH	The product is no dispersible	A	"
830.7300	Density (Bulk Density)	1.044	A	"

A = Acceptance, NA = Not Acceptable, G = Data Gap, W = Waiver request,
N/A = Not applicable, I = In progress

CONCLUSIONS:

1. TRB has reviewed the CSFs for the proposed basic (dated: 08/25/2010) and alternate formulations and has found them to be acceptable provided the product chemistry data for the source of the active ingredient Flumerthrin Technical is found to be acceptable for registration. The CSFs are attached with this review and can be located in OPPIN CHEM DOCS.

2. Product chemistry Group **A** and Group B data, with the exception of one year storage stability (830.6317) & corrosion characteristics (830.6320) are satisfied and acceptable.

3. The registrant must generate one year storage stability (830.6317) and corrosion characteristics (830.6320) data on the proposed product. It is required that the observations be made at 0, 3, 6, 9, and 12 month intervals. The results must be submitted to the Agency in electronic and hard copy format.

4. The proposed label was screened as it pertains to the product chemistry requirements. The final review of the proposed label and uses are the purview of the PM team.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	EPA Reg No./File Symbol: 11556-RLL	Page 1 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Flumethrin Active Ingredient Specific (Pages 1 – 7)						
Product Chemistry, Section 158.300						
830.1550	Product identity and Composition	48240201	11556	OWN	23979 (BR 2625)	
830.1600	Description of materials used to produce the product	48240201	11556	OWN	23979 (BR 2625)	
830.1620	Description of production process	48240201	11556	OWN	23979 (BR 2625)	
830.1650	Description of formulation process					N.A. - EP Only
830.1670	Discussion on formation of impurities	48240201	11556	OWN	23979 (BR 2625)	
830.1700	Preliminary analysis	48240201	11556	OWN	23979 (BR 2625)	
830.1750	Certified of limits	48240201	11556	OWN	23979 (BR 2625)	
830.1800	Enforcement method	48240201	11556	OWN	23979 (BR 2625)	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color	48240202	11556	OWN	23980 (BR 2624)	
830.6303	Physical state	48240202	11556	OWN	23980 (BR 2624)	
830.6304	Odor	48240202	11556	OWN	23980 (BR 2624)	
830.6313	Stability	48240202	11556	OWN	23980 (BR 2624)	
830.6314	Oxidizing / reducing action	48240202	11556	OWN	23980 (BR 2624)	
830.6315	Flammability	48240202	11556	OWN	23980 (BR 2624)	
830.6316	Explodability	48240202	11556	OWN	23980 (BR 2624)	
830.6317	Storage stability	48240202	11556	OWN	23980 (BR 2624)	
830.6319	Miscibility	48240202	11556	OWN	23980 (BR 2624)	
830.6320	Corrosion characteristics	48240202	11556	OWN	23980 (BR 2624)	
830.6321	Dielectric breakdown volt	48240202	11556	OWN	23980 (BR 2624)	
830.7000	pH	48240202	11556	OWN	23980 (BR 2624)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 2 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.7050	UV/Visible absorption	48240202	11556	OWN	23980 (BR 2624)	
830.7100	Viscosity	48240202	11556	OWN	23980 (BR 2624)	N.A. – Not a liquid
830.7200	Melting point	48240202	11556	OWN	23980 (BR 2624)	
830.7220	Boiling point	48240202	11556	OWN	23980 (BR 2624)	
830.7300	Density, bulk-density, or specific gravity	48240202	11556	OWN	23980 (BR 2624)	
830.7370	Dissociation constant in water	48240202	11556	OWN	23980 (BR 2624)	N.A. – Does not dissociate
830.7520	Particle size, fiber length, and diameter distribution	48240202	11556	OWN	23980 (BR 2624)	
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)	48240202	11556	OWN	23980 (BR 2624)	
830.7840 830.7860	Water solubility	48240202	11556	OWN	23980 (BR 2624)	
830.7950	Vapor pressure	48240202	11556	OWN	23980 (BR 2624)	
Terrestrial and aquatic non-target organisms data requirements, Section 158.630						
850.2100	Avian oral toxicity					N.A.
850.2200	Avian dietary toxicity					N.A.
850.2400	Wild mammal toxicity					N.A.
850.2300	Avian reproduction					N.A.
850.2500	Simulated or actual field testing					N.A.
850.1075	Freshwater fish toxicity					N.A.
850.1010	Acute toxicity freshwater invertebrates					N.A.
850.1025 850.1035 830.1045 830.1055 830.1075	Acute toxicity estuarine and marine organisms					N.A.
850.1300	Aquatic invertebrates life cycle (freshwater)					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 3 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
850.1350	Aquatic invertebrates life cycle (saltwater)					N.A.
850.1400	Fish early-life stage (freshwater)					N.A.
850.1400	Fish early-life stage (saltwater)					N.A.
850.1500	Fish life cycle					N.A.
850.1710 850.1730 850.1850	Aquatic organisms bioavailability, biomagnifications, toxicity					N.A.
850.1950	Simulated or actual field testing for aquatic organisms					N.A.
850.1735	Whole sediment: acute freshwater invertebrates					N.A.
850.1740	Whole sediment: acute marine invertebrates					N.A.
850.3020	Honey bee acute contact toxicity					N.A.
850.3030	Honey bee toxicity of residues on foliage					N.A.
850.3040	Field testing for pollinators					N.A.
Toxicology, Section 158.500						
870.1100	Acute oral toxicity – rat	48240203	11556	OWN	76064 (ID 23940)	
		48240204	11556	OWN	14838	Supplemental
		48240205	11556	OWN	18186	Supplemental
870.1200	Acute dermal toxicity	48240206	11556	OWN	76065 (ID 23941)	
		48240207	11556	OWN	14837	Supplemental
870.1300	Acute inhalation toxicity – rat	48240208	11556	OWN	16302	
		48240209	11556	OWN	17815	Pilot study
		48240210	11556	OWN	17817	Pilot study

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protecćon Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 4 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.2400	Primary eye irritation – rabbit	48240211	11556	OWN	33853	Waiver request
		48240212	11556	OWN	14967	Supplemental Study
870.2500	Primary dermal irritation	48240213	11556	OWN	76066 (ID 23942)	
870.2600	Dermal sensitization	48240214	11556	OWN	14561	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate
870.6200	Acute neurotoxicity - rat	48240215	11556	OWN	201861 (ID 32545)	N.R. – Not an organophosphate
870.3100	90-day oral - rodent					No oral exposure
870.3150	90-day feeding - non-rodent					N.R. – Nonfood use
870.3200	21-day dermal - rabbit/rat					N.R. – Nonfood use
870.3250	90-day dermal toxicity	48240216	11556	OWN	32570	
		48240217	11556	OWN	30932	Pilot study for 32570
		48240218	11556	OWN	30931	Pilot study for 32570 and 30932
870.3465	90-day inhalation	48240219	11556	OWN	18177	
870.6100	28-day delayed neurotoxicity - hen					N.R. – Not an organophosphate
870.6200	90-day neurotoxicity - rat	48240220	11556	OWN	201706 (ID 32054)	
870.4100	Chronic oral toxicity - rodent	48240221	11556	OWN	19360	Listed as study type 870.4300 (combined)
		48240222	11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – rat	48240221	11556	OWN	19360	Listed as study type 870.4300 (combined)
		48240222	11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – mouse	48240223	11556	OWN	19383	See protocol discussion
		48240224	11556	OWN	18255	Pilot study for ID 19383
870.3700	Developmental toxicity - rat	48240225	11556	OWN	18968	
870.3700	Developmental toxicity – rabbit	48240226	11556	OWN	35286	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 5 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.3800	Reproduction and fertility effects	48240227	11556	OWN	32775	
		48240228	11556	OWN	13252	Pilot study for 32775
		48240229	11556	OWN	30322	Pilot study for 32775
		48240230	11556	OWN	30686	Pilot study for 32775
		48240231	11556	OWN	30517	Supplement to 30686
870.6300	Developmental neurotoxicity	48240232	11556	OWN	201747 (ID 32365)	
870.5100	Bacterial reverse mutation assay	48240233	11556	OWN	14173	
		48240234	11556	OWN	14174	
		48240235	11556	OWN	30687	
870.5300 870.5375	*In vitro* mammalian cell assay	48240236	11556	OWN	15461	
		48240237	11556	OWN	31492	
		48240238	11556	OWN	74691 (ID 16145)	
		48240239	11556	OWN	31489	
870.5385 870.5395	*In vitro* cytogenetics	48240240	11556	OWN	30951	
		48240241	11556	OWN	15198	
870.5550	Unscheduled DNA Synthesis	48240242	11556	OWN	14867	
870.7485	Metabolism and pharmacokinetics	48240243	11556	OWN	14368	
		48240244	11556	OWN	22813	
		48240245	11556	OWN	30971	
		48240246	11556	OWN	15839	Cattle – Supplemental Study
		48240247	11556	OWN	22818	Sheep – Supplemental Study
		48240248	11556	OWN	22819	Sheep – Supplemental Study
		48240249	11556	OWN	15987	Cattle – Supplemental Study
870.7200	Companion animal safety					N.A. for EP Only
870.7600	Dermal penetration					N.R. – See Risk Assessment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 6 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.7800	Immunotoxicity	48240250	11556	OWN	35217	
875.2400	Post-Application Exposure (Dermal)					N.A. EP Only
None	1998 EMEA Summary/Overview on Flumethtrin	48240251	11556	OWN	35038	Requested by Agency in Pre-Reg Meeting of 11/11/06
Environmental Fate, Section 158.1300						
835.2120	Hydrolysis					N.A.
835.2240	Photodegradation - water					N.A.
835.2410	Photodegradation - soil					N.A.
835.2370	Photodegradation - air					N.A.
835.4100	Aerobic soil metabolism					N.A.
835.4200	Anaerobic soil metabolism					N.A.
835.4300	Aerobic aquatic metabolism					N.A.
835.4400	Anaerobic aquatic metabolism					N.A.
835.1230 835.1240	Leaching / adsorption/desorption					N.A.
835.1410	Volatility - laboratory					N.A.
835.8100	Volatility - field					N.A.
835.6100	Terrestrial field dissipation					N.A.
835.6200	Aquatic (sediment)					N.A.
835.6300	Forestry					N.A.
835.6400	Combination and tank mixes					N.A.
835.7100	Ground water monitoring					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 7 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Residue Chemistry, Section 158.1410						
	Nature of residue - plants					N.A.
	Nature of residue - livestock and poultry					N.A.
	Residue analytical method - plants					N.A.
	Residue analytical method - animal					N.A.
	Storage stability					N.A.
	Magnitude of residues - meat/milk/poultry/egg					N.A.
	Magnitude of residue - crop field trials					N.A.
	Magnitude of residue - processed food/feed					N.A.
	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.
810.3300	Treatments to control pests of humans and pets					N.A. for EP Only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 8 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Imidacloprid Active Ingredient Specific (Pages 8 – 14)						
Product Chemistry, Section 158.240						
61-1	Chemical identity	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
61-2	Statement of Composition	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
		42270801	264	PER	BR 1785 (TGAI)	
61-3	Formation of impurities	42055302	264	PER	BR 1759 (TGAI)	
62-1	Preliminary analysis	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
		42270802	264	PER	BR 1786 (TGAI)	
62-2	Certification of limits	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
62-3	Analytical method	42055303	264	PER	BR 1760 (TGAI)	
		43213001	264	PER	BR 1874 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
63-1	Chemical and Physical Properties	42055304	264	PER	BR 1761 (TGAI)	
63-2	Appearance	42055304	264	PER	BR 1761 (TGAI)	
63-3	Physical state	42055304	264	PER	BR 1761 (TGAI)	
63-4	Odor	42055304	264	PER	BR 1761 (TGAI)	
63-5	Melting point	42055304	264	PER	BR 1761 (TGAI)	
63-6	Boiling point	42055304	264	PER	BR 1761(TGAI)	
63-7	Density	42055304	264	PER	BR 1761 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 9 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
63-8	Solubility	42055304	264	PER	BR 1761 (TGAI)	
63-9	Vapor pressure	42055304	264	PER	BR 1761 (TGAI)	
63-10	Dissociation constant					N.A. - Does not dissociate
63-11	Octanol / water partition	42055304	264	PER	BR 1761 (TGAI)	
63-12	pH	42055304	264	PER	BR 1761 (TGAI)	
63-13	Stability	42055304	264	PER	BR 1761 (TGAI)	
63-14	Oxidizing / reducing action					N.A. - No oxidative or reductive characteristics
63-15	Flammability	42055304	264	PER	BR 1761 (TGAI)	
63-16	Explodability	42055304	264	PER	BR 1761 (TGAI)	
63-17	Storage stability	42055304	264	PER	BR 1761 (TGAI)	
63-18	Viscosity					N.A. - Solid
63-19	Miscibility					N.A. - Solid
63-20	Corrosion characteristics	42055304	264	PER	BR 1761 (TGAI)	
63-21	Dielectric breakdown volt					N.A.- Solid
64-1	Submittal of samples				Samples available upon request	
Wildlife and Aquatic Organisms, Section 158.490						
71-1	Acute avian oral - quail/duck					N.A.
71-2(a)	Avian dietary - quail					N.A.
71-2(b)	Avian dietary - duck					N.A.
71-3	Wild mammal toxicity					N.A.
71-4(a)	Avian reproduction - quail					N.A.
71-4(b)	Avian reproduction – duck					N.A.
71-5	Simulated or actual field study					N.A.
72-1(a)	Fish toxicity - bluegill					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 10 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
72-1(b)	Fish toxicity bluegill - tep					N.A.
72-2(a)	Invertebrate toxicity - Daphnia					N.A.
72-2(b)	Invertebrate toxicity - Amphipods					N.A.
72-2(e)	Acute aquatic invertebrate toxicity - Chironomids					N.A.
72-3(a)	Estuarine / marine toxicity - fish					N.A.
72-3(b)	Estuarine / marine toxicity - mollusk					N.A.
72-3(c)	Estuarine/marine toxicity - shrimp					N.A.
72-4(a)	Early life stage - fish					N.A.
72-4(b)	Life cycle invertebrate					N.A.
72-7	Simulated or actual field study					N.A.
None	Foliar half-life and distribution for potatoes					N.A.
None	Runoff and Erosion predictions for apple/potato/cotton					N.A.
None	Risk assessment for apple/potato/cotton					N.A.
Toxicology, Section 158.340						
81-1	Acute oral toxicity rat	42055331	264	PER	Report No. 100040 (TGAI)	
81-2	Acute dermal toxicity, rat/rabbit	42055332	264	PER	Report No. 100041 (TGAI)	
81-3	Acute inhalation toxicity, rat	42055333	264	PER	Report No. 99806 (TGAI)	
		42286101	264	PER	Report No. 99806-1 (TGAI)	
81-4	Primary eye irritation - rabbit	42055334	264	PER	Report No. 99679 (TGAI)	
81-5	Primary dermal irritation - rabbit	42055335	264	PER	Report No. 99804 (TGAI)	
81-6	Dermal sensitization - guinea pig	42055336	264	PER	Report No. 99800 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 11 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
		43170301	264	PER	Report No. 106348	
		43285801	264	PER	Report No. 106348-1	
81-8(SS)	Acute neuratoxicily	42770301	264	PER	Report No. 103979	
82-1(a)	90-day feeding - rodent	42256327	264	PER	Report No. 100036	
82-1(b)	90-day feeding - non-rodent	42256328	264	PER	Report No. 100176	
		42256329	264	PER	Report No. 100688	
82-2	21-day dermal - rabbit/rat	48024009	264	PER	Report No. M-357205	
82-5(b)	90 day neurotoxicity - mammal	43286401	264	PER	Report No. 106356	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-1(a)	Chronic feeding toxicity - rodent	42256334	264	PER	Report No. 99672	
83-1(b)	Chronic feeding toxicity - non-rodent	42273002	264	PER	Report No. 100015	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-2(a)	Oncogenicity - rat	42256334	264	PER	Report No. 99672	
		42256335	264	PER	Report No. 100693	
		42256336	264	PER	Report No. 101929	
83-2(b)	Oncogenicity - mouse	42256337	264	PER	Report No. 99808	
83-3(a)	Developmental toxicity - rat	42256338	264	PER	Report No. 98571	
83-3(b)	Developmental toxicity - rabbit	42256339	264	PER	Report No. 98572	
83-4	Two generation reproduction - rat	42256340	264	PER	Report No. 100647	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 12 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
84-2(a)	Gene mutation (ames test)	42256341	264	PER	Report No. 101276	
		42256342	264	PER	Report No. 98584	
		42256343	264	PER	Report No. 98570	
84-2(b)	Structural chromosomal aberration	42256344	264	PER	Report No. 100021	
		42256345	264	PER	Report No. 99262	
		42256346	264	PER	Report No. 99257	
		42256347	264	PER	Report No. 102652	
		42256348	264	PER	Report No. 102654	
		42256349	264	PER	Report No. 102655	
84-4	Other genotoxic effects	42256350	264	PER	Report No. 99676	
		42256351	264	PER	Report No. 101275	
		42256352	264	PER	Report No. 98573	
		42256353	264	PER	Report No. 102653	
85-1	General metabolism	42256354	264	PER	Report No. 101999	
		42256355	264	PER	Report No. 87264	
		42256356	264	PER	Report No. 87265	
		42256357	264	PER	Report No. 102617	
870.7200 (86-1)	Domestic Animal Safety					N.A. for EP Only
95-9	Efficacy					N.A. for EP Only
Plant Protection, Section 158.540						
122-2	Aquatic plant growth					N.A.
123-2	Aquatic plant growth					N.A.
141-1	Honey bee acute contact					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 13 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
141-2	Honey bee residue on foliage					N.A.
Reentry Protection, Section 158.390						
230-236	Mixer/loader/applicator exposure	42256386 43790701	264 11556	PER OWN	Report No. 94273 Report No. 106743	
Environmental Fate, Section 158.290						
161-1	Hydrolysis					N.A.
161-2	Photodegradation - water					N.A.
161-3	Photodegradation - soil					N.A.
162-1	Aerobic soil metabolism					N.A.
162-2	Anerobic soil metabolism					N.A.
162-3	Anaerobic aquatic metabolism					N.A.
163-1	Leaching / adsorption/desorption					N.A.
164-1	Terrestrial field dissipation					N.A.
165-1	Confined rotational crop					N.A.
165-2	Field rotational crop					N.A.
166-1	Ground water - small prospective					N.A.
None	Environmental fate summary					N.A.
Residue, Section 158.240						
171-4(a)	Nature of residue - plants					N.A.
171-4(b)	Nature of residue - livestock and poultry					N.A.
171-4(c)	Residue analytical method - plants					N.A.
171-4(d)	Residue analytical method - animal					N.A.
171-4(e)	Storage stability					N.A.
171-4(j)	Magnitude of residues - meat/milk/poultry/egg					N.A.
171-4(k)	Magnitude of residue - crop field trials					N.A.
171-4(l)						N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 14 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Magnitude of residue - processed food/feed					
171-4(m)	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** t1556-RLL	Page 15 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
PNR 1427 Insecticide End-Use Product Specific (Pages 15 – 18)						
Product Chemistry, Section 158.240						
830.1550	Product identity and Composition	48240101	11556	OWN	33752	
830.1600	Description of materials used to produce the product	48240101	11556	OWN	33752	
830.1620	Description of production process	48240101	11556	OWN	33752	
830.1650	Description of formulation process	48240101	11556	OWN	33752	
830.1670	Discussion on formation of impurities	48240101	11556	OWN	33752	
830.1700	Preliminary analysis					N.A. TGAI Only
830.1750	Certified of limits	48240101	11556	OWN	33752	
830.1800	Enforcement method	48240101	11556	OWN	33752	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color	48240101	11556	OWN	33752	
830.6303	Physical state	48240101	11556	OWN	33752	
830.6304	Odor	48240101	11556	OWN	33752	
830.6313	Stability					N.A. – TGAI Only
830.6314	Oxidizing / reducing action					N.A.– EP not contain an oxidizing or reducing agent
830.6315	Flammability					N.R. – This product is not considered a combustible liquid, because the closed up flashpoint for all the ingredients is > 199°F.
830.6316	Explodability					N.R. – This product does not contain any explosive ingredients.
830.6317	Storage stability					Pending; Available 3/31/2011
830.6319	Miscibility					N.R. – This product is not an emulsifiable type

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 16 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.6320	Corrosion characteristics					Pending; Available 3/31/2011
830.6321	Dielectric breakdown volt					N.A. – Not intended use around electrical equipment
830.7000	pH					N.A. – product not soluble in water and therefore pH not required.
830.7050	UV/Visible absorption					N.A. – TGAI Only
830.7100	Viscosity					N.A. – This product is a solid and viscosity is not applicable.
830.7200	Melting point					N.A.– TGAI Only
830.7220	Boiling point					N.A. – TGAI Only
830.7300	Density, bulk-density, or specific gravity					
830.7370	Dissociation constant in water					N.A. – TGAI Only
830.7520	Particle size, fiber length, and diameter distribution					N.A. – Nonfiberous product
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)					N.A. – TGAI Only
830.7840 830.7860	Water solubility					N.A. – TGAI Only
830.7950	Vapor pressure					N.A. – TGAI Only
Toxicology, Section 158.500						
870.1100	Acute oral toxicity - rat	48240102	11556	OWN	33854	Waiver request
870.1200	Acute dermal toxicity	48240103	11556	OWN	33855	Waiver request
870.1300	Acute inhalation toxicity - rat	48240104	11556	OWN	33856	Waiver request
870.2400	Primary eye irritation – rabbit	48240105	11556	OWN	33857	Waiver request
870.2500	Primary dermal irritation	48240106	11556	OWN	33749	
870.2600	Dermal sensitization	48240107	11556	OWN	33750	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 17 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.6200	Acute neurotoxicity - rat					N.R. – Not an organophosphate
870.3100	90-day oral - rodent					N.R.
870.3200	21-day dermal - rabbit/rat					N.R. – Non-food use
870.3250	90-day dermal					N.R. – Collar not affect uptake
870.7200	Companion animal safety	48240108	11556	OWN	33800	Adult cat safety study
		48240108	11556	OWN	33826	Amendment to adull cat study 33800
		48240109	11556	OWN	33805	Adult dog safety study
		48240110	11556	OWN	33806	Puppy safety study
		48240111	11556	OWN	33824	Kitten safety study
		48240112	11556	OWN	33822	Reflector study (puppy)
		48240113	11556	OWN	33823	Reflector study (kitten)
		48240114	11556	OWN	35986	Reflector study (adult cat)
		48240115	11556	OWN	35637	Reflector Study (adult dog)
Product Performance, Section 158.400						
810.3300	Treatments to control pests of humans and pets					
		48240116	11556	OWN	33801	Fleas and ticks (dogs)
		48240117	11556	OWN	33802	Fleas and ticks (cats)
		48240118	11556	OWN	33803	Efficacy with bathing and water immersion against ticks and fleas
		48240119	11556	OWN	35630	Fleas and ticks [Ixodes ricinis] (cats)
		48240120	11556	OWN	35631	Adult and larvacidal flea control; repellency and tick control (dogs)
		48240121	11556	OWN	35635	Adult and larvacidal fleas, ticks study (cats)
		48240122	11556	OWN	35644	Field studies – fleas and ticks (cats)
		48240123	11556	OWN	35645	Field studies– fleas and ticks (dogs)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 18 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Treatments to control pests of pets (cont'd)	48240124	11556	OWN	35980	Speed of kill for fleas (cats)
		48240125	11556	OWN	35987	Speed of kill for fleas (dogs)
		48240126	11556	OWN	33464	Ixodes Bridging study
		48240127	11556	OWN	35981	Ticks [Ixodes ricinis] (cats)
		48240128	11556	OWN	35979	Ticks [Ixodes ricinis] (dogs)
		48240129	11556	OWN	35982	Repellency and control of ticks (dogs)
		48240130	11556	OWN	33467	Juvenile Ticks
		48240131	11556	OWN	33694	Lice (Trichodectes canis)
		48240132	11556	OWN	33691	Sarcoptic mange
		48240133	11556	OWN	36172	Hair clipping study – Repellency and efficacy
		48240134	11556	OWN	15962	Hair clipping study
		48240135	11556	OWN	35642	Serum and haircoat kinetics in cats
		48240136	11556	OWN	35643	Serum and haircoat kinetics in dogs
		48240137	11556	OWN	15749	Advantage Efficacy against C. canis
Miscellaneous						
None	Benefits Document (In the Public Interest)	48240138	11556	OWN	33860	Submitted w/ Flumethrin Technical Application
None	ORE Risk Assessment	48240139	11556	OWN	33861	
None	Release Rate Compilation	48240140	11556	OWN	35992	
None	Soluble Surface Content of Collar	48240141	11556	OWN	35118	

Signature Douglas A. Spilker

Douglas A. Spilker
Manager, EPA Regulatory Affairs

8 Nov. 2010

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

December 02, 2011

BAYER HEALTHCARE LLC
PO.BOX : 390
SHAWNEE MISSION, KS 66201-0390

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 30-NOV-11. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

48674700

Bayer HealthCare
Animal Health

Via Federal Express

November 29, 2011

Document Processing Desk (ADDL DATA - NO REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Mr. Richard Gebken/PM10
Registration Division (7505P)

Subject: PNR1427 Insecticide (EPA File Symbol 11556-RLL)
Amendments to Companion Animal Safety Studies

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Dear Mr. Gebken:

Please find enclosed two respective amendments to currently on-file companion animal safety studies on adult cats and adult dogs. The enclosed amendments provide additional information about the required studies, as requested in a teleconference on this subject with the Agency on October 20, 2011 (Dr. Byron Backus and Ms. BeWanda Alexander.) The main objective of these amendments is to appropriately recalculate the exposure of the target animals to the levels of the two active ingredients released from the collars worn by the pets during the study.

We will update the respective Data Matrix and resubmit it after we receive the MRID numbers back from the Agency. If you have any questions, please do not hesitate to call me at 913-268-2751.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures:

1. Bayer Report No. 33967 – *Adult Dogs* (3 copies)
2. Bayer Report No. 33968 – *Adult Cats* (3 copies)

Transmittal Document

1. Name and Address of Submitter
Bayer HealthCare LLC
Animal Health Division
Box 390
Shawnee Mission, Kansas 66201-0390

Douglas A. Spilker, Ph.D.
Manager, EPA Regulatory Affairs
(913) 268-2751

2. Regulatory Action in Which this Package is Submitted
Additional Information for the Pending Application for Registration of "PNR1427 Insecticide"; File Symbol 11556-RLL

3. Transmittal Date
November 29, 2011

4. List of Submitted Studies:

MRID No.	Volume		
48674701	1	-	"*Final Report Amendment 1 to Bayer Report 33805 (MRID 48240109) – Safety of PNR 1427 in Adult Dogs*," Bayer Report No. 33967, Harish M. Chopade, 16 pp.
48674702	2	-	"*Final Report Amendment 2 to Bayer Report 33800 (MRID 48240108) – Safety of PNR 1427 in Adult Cats*," Bayer Report No. 33968, Harish M. Chopade, 16 pp.

Memorandum

Date: 12/06/11

To: RM 10, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- ☑ fully accepted submission
- ☐ partially accepted submission
- ☐ rejected submission

Bayer HealthCare
Animal Health

Via Federal Express

March 10, 2011

Document Processing Desk (ADDL DATA - NO REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Mr. Richard Gebken/PM10
Registration Division (7505P)

Subject: PNR1427 Insecticide (EPA File Symbol 11556-RLL)

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Dear Mr. Gebken:

Please find enclosed a study providing data to fulfill the data requirements of one year storage stability (OPPTS GL No. 830.6317) and corrosion characteristics (OPPTS GL No. 830.6320) in support of the pending registration of the subject product. As requested, please also find an electronic version of this report on the enclosed CD. **Please note that the title of the report refers to "M915 Insecticide," the previous code name for the product, but the formulation being the same.**

I will update the respective Data Matrix and resubmit it after I receive the MRID number back from the Agency.

If you have any questions, please do not hesitate to call me at 913-268-2751.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures:

1. Bayer Report No. 33906 (3 copies paper; 1 copy CD)

cc: B. Alexander (EPA) - email

Transmittal Document

1. Name and Address of Submitter
Bayer HealthCare LLC
Animal Health Division
Box 390
Shawnee Mission, Kansas 66201-0390

Douglas A. Spilker, Ph.D.
Manager, EPA Regulatory Affairs
(913) 268-2751

2. Regulatory Action in Which this Package is Submitted
Submission of one year storage stability (830.6317) and corrosion characteristics (830.6320) report, in support of the pending registration of PNR1427 Insecticide (EPA File Symbol 11556-RLL)

3. Transmittal Date
March 10, 2011

4. List of Submitted Studies:

MRID No.	Volume	
48416501	1	- *Evaluation of Stability and Corrosion Characteristics of M915 Insecticide,* OPPT 830.6317 and 830.6320; Bayer Report No. 33906, Rose, J., 24 pp. (3 paper copies; 1 CD)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

October 6, 2010

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

BAYER HEALTHCARE LLC
ANIMAL HEALTH DIVISION
PO Box 390
SHAWNEE MISSION, KS 66201-0390

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 24-SEP-10. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

482401

Bayer HealthCare
Animal Health

Via Federal Express

September 23, 2010

Document Processing Desk (REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Mr. Richard Gebken/PM10
Registration Division (7505P)

Subject: Application for Registration of a New Active Ingredient (PRIA R110): **Flumethrin Technical (CAS No. 69770-45-2)**

Application for Registration of a Combination (Flumethrin + Imidacloprid) End-Use Product: ***PNR1427 Insecticide***

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-039

Dear Mr. Gebken:

With this application, the enclosed data and labeling, Bayer HealthCare LLC, Animal Health Division (BAH) is requesting the registration of a new technical active ingredient – "*Flumethrin Technical*" containing **flumethrin** (CAS No. 69770-45-2). A second application for registration of *PNR1427 Insecticide* end-use product (flea and tick pet collar) is being submitted concurrently with this application for registration of the technical active ingredient. The flumethrin technical active ingredient, which is also the manufacturing-use product, is for formulation purposes ONLY into products with indoor, non-food uses. The "specific use pattern" on domestic animals, according to the Pesticide Use Index, is determined to be Group Number 99 "Indoor – Non-Food."

The proposed *Flumethrin Technical* is considered a "new" active ingredient in that it is "...not currently contained as an active ingredient in any EPA registered pesticide product." The ultimate use of this technical active ingredient is for formulation into pesticide products on pets (cats and dogs), which are considered indoor use patterns by the Agency. No flumethrin-containing end-use products are proposed that would be used on or come into contact with food and/or feed items. Therefore as described in the PRIA Decision Tree, the application for registration of this new active ingredient – *Flumethrin Technical* - falls under the action code **R110: "Nonfood use; Indoor."** Furthermore, it is our understanding that all indoor non-food use products included with this technical active

ingredient application are covered by the base fee in this category, if submitted simultaneously. The application for the end-use product, *PNR1427 Insecticide*, is being submitted simultaneously with the technical product application, and therefore there should be no additional PRIA fee for the *PNR1427 Insecticide* application.

Flumethrin, a new active ingredient, is intended as a Technical/ Manufacturing Use Product for formulating insecticides for indoor uses (on domestic animals; cats and dogs). *Flumethrin Technical* is proposed for use in combinations with other EPA-registered active ingredients (such as imidacloprid). *PNR1427 Insecticide* is a new pesticide end-use product combining two active ingredients, imidacloprid and flumethrin, in a pet collar formulation. It is intended for the prevention and treatment of public health pests, such as ticks and fleas, on kittens, cats, puppies and dogs.

The Agency is not unfamiliar with this active ingredient and end-use product, as Bayer Healthcare has had several pre-registration meetings and/or teleconferences with the Agency to discuss these registration actions and the specific 40 CFR Part 158 requirements for these products. Detailed overviews of the two actions are attached to the respective Applications for Pesticide Registration (EPA Form No. 8570-1), and the Bayer-EPA interactions will be referenced in the respective sections of these overviews, and copies of referenced documents provided. We **request that copies of the two applications with attachments be forwarded to the respective review groups, as we think this information could be quite helpful during their review processes.**

Information regarding the benefits of this new active ingredient-containing product is contained in the document entitled: "Benefits of Flumethrin Active Ingredient and the Imidacloprid/Flumethrin Collar for Cats and Dogs (PNR1427), Bayer report No. 33860," which should allow the Agency to make the determination that "...the use of the pesticide will not cause any unreasonable risk to the environment; and the use of the pesticide is in the public interest."

If you have any questions, please do not hesitate to call me at 913-268-2751.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures:

1. Copy of Check – Check No. 2000542090 ($209,475.00), cover letter, dated 9/20/10, and delivery confirmation, dated 9/21/2010

2. **Application for Registration – *Flumethrin Technical***

    a. Administrative Volume (Volume 1 on Transmittal Document)
        i. Cover letter (Extra Copy)
        ii. Copy of PRIA Payment (Check No. 2000542090)
        iii. Application for Registration – Flumethrin Technical (Form 8570-1), 10pp. w/ 6 attachments
        iv. Transmittal document
        v. Confidential Statement of Formula, dated 11/15/2008 (2 copies)
        vi. Certification with Respect to Citation of Data (Form 8570-34)
        vii. Data Matrix (CONFIDENTIAL) – "Flumethrin Active Ingredient Specific, dated 9/20/2010," 7pp.
        viii. Data Matrix (PUBLIC) – "Flumethrin Active Ingredient Specific, dated 9/20/2010," 7pp.
        ix. Product label, dated 9/20/2010 (3 copies)
    b. Bayer Reports – ID Nos. 23979, 23980, 23940, 14838, 18186, 23941, 14837, 16302, 17815, 17817, 33853, 14967, 76066, 14561, 32545, 32570, 30932, 30931, 18177, 201706, 19360, 15285, 19383, 18255, 18968, 35286, 32775, 13252, 30322, 30686, 30517, 32365, 14173, 14174, 30687, 15461, 31492, 74691, 31489, 30951, 15198, 14867, 14368, 22813, 30971, 15839, 22818, 22819, 15987, 35217, 35038 (3 copies each)

3. **Application for Registration – end-use product *PNR1427 Insecticide***

    a. Administrative Volume (Volume 1 on Transmittal Document)
        i. Cover letter (Extra Copy)
        ii. Application for Registration – PNR1427 Insecticide (Form 8570-1), 17pp. w/ 7 attachments
        iii. Confidential Statements of Formula (3) – Basic, Alt 1, and Alt 2, dated 8/25/2010; 2 copies each)
        iv. Transmittal Document
        v. Certification with Respect to Citation of Data (Form 8570-34)

vi. Letter of Authorization from Bayer CropScience (for imidacloprid), dated 9/7/2010
vii. Data Matrix (CONFIDENTIAL) – PNR1427 Insecticide: "Flumethrin Active Ingredient Specific (pages 1-7), Imidacloprid Active Ingredient Specific (pages 8-14), and PNR1427 Insecticide Specific (pages 15-18); dated 9/20/2010," total pages – 18
viii. Data Matrix (PUBLIC) – PNR1427 Insecticide: "Flumethrin Active Ingredient Specific (pages 1-7), Imidacloprid Active Ingredient Specific (pages 8-14), and PNR1427 Insecticide Specific (pages 15-18); dated 9/20/2010," total pages -18
ix. Product label, dated 9/20/2010 (3 copies)

b. Bayer Reports – ID Nos. 33752, 33854, 33855, 33856, 33857, 33749, 33750, 33800, 33826, 33805, 33806, 33824, 33822, 33823, 35986, 35637, 33801, 33802, 33803, 35630, 35631, 35635, 35644, 35645, 35980, 35987, 33464, 35981, 35979, 35982, 33467, 33694, 33691, 36172, 15962, 35642, 35643, 15749, 33860, 33861, 35992, 35118 (3 copies each)

TRANSMITTAL DOCUMENT

Name and Address of Submitter:	Bayer HealthCare LLC Animal Health Division Box 390 Shawnee Mission, Kansas 66201-0390
Regulatory action in support of which this package is submitted:	Application for registration of **PNR1427 Insecticide**
EPA Reg. No./File Symbol:	Company Number: 11556- XXX
Alternate Test Material Names:	N/A
Transmittal Date:	September 23, 2010
Box Count:	**19 – 24**

Volume Number	Citation	MRID Number
	Administrative Materials - Cover letter (Extra Copy) - Application for Pesticide Registration (with Attachments) - Confidential Statement of Formula (2 copies) - Transmittal Document - Certification with respect to Citation of Data (8570-34) - Letter of Authorization from Bayer CropScience (imidacloprid) - Data Matrix (CONFIDENTIAL) - Data Matrix (PUBLIC) - Product Label (3 copies)	
2	Rose, J.E., 2009, Chemistry Evaluation of M915 Insecticide, 33752 (1 book, 3 copies).	**48240101**
3	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Oral Toxicity Study – PNR 1427 Insecticide, 33854 (1 book, 3 copies).	**48240102**
4	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Dermal Toxicity Study – PNR 1427 Insecticide, 33855 (1 book, 3 copies).	**48240103**
5	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Inhalation Toxicity Study – PNR 1427 Insecticide, 33856 (1 book, 3 copies).	**48240104**
6	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Eye Irritation Toxicity Study – PNR 1427 Insecticide, 33857 (1 book, 3 copies).	**48240105**
7	Durando, J., 2009, Primary Skin Irritation Study in Rabbits, 33749 (1 book, 3 copies).	**48240106**

Volume Number	Citation	MRID Number
8	Durando, J., 2009, Dermal Sensitization Study in Guinea Pigs (Buehler Method), 33750 (1 book, 3 copies).	48240107
9	Madsen, T.J., 2010, Safety of PNR 1427 in adult cats, 33800 (1 book, 3 copies).	48240108
10	Madsen, T.J., 2010, Amendment to Bayer Report No.33800-Safety of PNR1427 in Adult Cats, 33826 (1 book, 3 copies).	
11	Madsen, T.J., 2010, Safety of PNR 1427 in Adult Dogs, 33805 (1 book, 3 copies).	48240109
12	Madsen, T.J. & Chopade, H., 2010, Safety of PNR1427 in Puppies, 33806 (2 books, 3 copies).	48240110
13	Madsen, T.J., 2010, Safety of PNR 1427 in Kittens, 33824 (2 books, 3 copies).	48240111
t4	Madsen, T.J., 2010, Safety of PNR1427 With Reflectors in Puppies, 33822 (1 book, 3 copies).	48240112
15	Madsen, T.J., 2010, Safety of PNR1427 with Reflectors in Kittens, 33823 (1 book, 3 copies).	48240113
16	Delport, P.C., 2010, Target animal safety with a PNR 1427 collar with and without reflectors when applied once to adult cats, 35986 (1 book, 3 copies).	48240114
17	Bach, T., 2010, Target Animal Safety With A 10% Imidacloprid + 4.5% Flumethrin Collar With or Without Reflector Clips Applied Once To Adult Dogs, 35637 (1 book, 3 copies).	48240115
18	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Efficacy of PNR1427 Against Tick (Dermacentor variabilis, Rhipicephalus sanguineus) and Flea Infestations on Dogs, 33801 (1 book, 3 copies).	48240116
19	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Efficacy of PNR1427 Against Tick (Amblyomma americanum) and Flea Infestations on Cats, 33802 (1 book, 3 copies).	48240117
20	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Evaluation of the Effects of Shampooing or Water Immersion on the Efficacy of PNR1427 Against Flea (Ctenocephalides felis) and Tick (Dermacentor variabilis, Rhipicephalus sanguineus) Infestations on Dogs, 33803 (t book, 3 copies).	48240118
21	Strube, K., Stanneck, D., Schroeder, I., & Kruedewagen, E., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus) and flea (Ctenocephalides felis) infestations in cats, 35630 (1 book, 3 copies).	48240119

Volume Number	Citation	MRID Number
22	Strube, K., Stanneck, D., Schroeder, I., & Kruedewagen, E., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus and Rhipicephalus sanguineus) and flea (Ctenocephalides felis) infestations in dogs, 35631 (1 book, 3 copies).	**48240120**
23	Wolken, S., & Stanneck, D., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus) and flea (Ctenocephalides felis) infestations in cats, 35635 (1 book, 3 copies).	**48240121**
24	Rass, J. & Stanneck, D., 2010, Evaluation of the Efficacy, Persistency and Safety of "Imidacloprid 10%/Flumethrin 4.5% Collar" in Cats Naturally Infested with Fleas and/or Ticks in a Multi-Centric Clinical Field Study in the EU, 35644 (1 book, 3 copies).	**48240122**
25	Rass, J. & Stanneck, D., 2010, Evaluation of the Efficacy, Persistency and Safety of "Imidacloprid 10%/Flumethrin 4.5% Collar" in Dogs Naturally Infested with Fleas and/or Ticks in a Multi-Centric Clinical Field Study in the EU, 35645 (1 book, 3 copies).	**48240123**
26	Strube, K. & Schroeder, I., 2010, Onset of Efficacy of a 10% Imidacloprid/ 4.5% Flumethrin Collar on Cats When Experimentally Infested with the Cat Flea Ctenocephalides felis (C. felis), 35980 (1 book, 3 copies).	**48240124**
27	Kok, D.J., 2010, Onset of Efficacy of an Imidacloprid/Flumethrin Collar Formulation Against Fleas (Ctenocephalides felis) on Dogs, 35987 (1 book, 3 copies).	**48240125**
28	Turberg, A. & Settje, T., 2010, Comparative in-vitro study of flumethrin efficacy against two Ixodes species in a glass vial contact assay, 33464 (1 book, 3 copies).	**48240126**
29	Strube, K., 2010, Onset of efficacy of a 10% Imidacloprid/ 4.5% flumethrin collar on cats when experimentally infested with *Ixodes ricinus (I. ricinus)*, 35981 (1 book, 3 copies).	**48240127**
30	Ketzis, J. & Schroeder, I., 2010, A controlled, randomized study to confirm the efficacy of Imidacloprid/Flumethrin containing collars against artificially induced infestations of Ixodes ricinus on beagles, 35979 (1 book, 3 copies).	**48240128**
31	Strube, K., 2010, Onset of Efficacy of a 10% Imidacloprid/ 4.5% Flumethrin Collar on Dogs when Experimentally Infested with *Ixodes ricinus* and *Rhipicephalus sanguineus*, 35982 (1 book, 3 copies).	**48240129**

Volume Number	Citation	MRID Number
32	Turberg, A., 2010, Comparative in-vitro study of efficacy of a 1 : 1.85 flumethrin : imidacloprid mixture against larvae, nymphs and adults of I. ricinus and R. sanguineus and larvae and adults of D. reticulatus ticks in a glass vial contact assay, 33467 (1 book, 3 copies).	**48240130**
33	Ketzis, J. & Stanneck, D., 2010, A Controlled, Randomized Study to Confirm the Efficacy of Imidacloprid/Flumethrin Containing Collars Against a Natural Infestation of Dog Lice (*Trichodectes canis*) on Mixed Bred and Purebred Dogs, 33694 (1 book, 3 copies).	**48240131**
34	Fourie, J.J., 2010, Evaluation of the Efficacy of an Imidacloprid/Flumethrin Collar Formulation on Dogs with Naturally Acquired Infestations of *Sarcoptes scabiei*, 33691 (1 book, 3 copies).	**48240132**
35	Kruedewagen, E., 2010, In-vitro Efficacy of Hair Coat Samples From Cats and Dogs Treated with Imidacloprid 10%/Flumethrin 4.5% Collars Against Ticks (*R. sanguineus*), 36172 (1 book, 3 copies).	**48240133**
36	Gyr, P. & Hopkins, T., 1995, Residues of BAY1 7391 10% w/v Spot-on in the Coat of Dogs at Various Times After Treatment, 15962 (1 book, 3 copies).	**48240134**
37	Delport, P.C., 2010, Serum and Hair Coat Kinetics of an Imidacloprid 10%/Flumethrin 4.5% Collar in Cats, 35642 (1 book, 3 copies).	**48240135**
38	Delport, P.C., 2010, Serum and Hair Coat Kinetics of an Imidacloprid 10%/Flumethrin 4.5% Collar in Dogs, 35643 (1 book, 3 copies).	**48240136**
39	Jacobs, D.E., 1995, Imidacloprid Spot-on 10% (BAY t 7391) for the Control of Fleas on Dogs - Clinical Field Study, 15749 (1 book, 3 copies).	**48240137**
40	Spilker, D.A., & Davis, W.L., 2010, "Benefits of Flumethrin Active Ingredient and the Imidacloprid/Flumethrin Collar for Cats and Dogs (PNR1427)", 33860 (1 book, 3 copies).	**48240138**
41	Lunchick, C., 2010, Occupational and Residential Exposure and Risk Assessment for PNR 1427 Dog and Cat Collars Formulated with Imidacloprid and Flumethrin, 33861 (1 book, 3 copies).	**48240139**
42	Stanneck, D., 2010, Dosage of the imidacloprid 10%/flumethrin 4.5% collar and release of the active ingredients over time in cats and dogs – Review Compilation, 35992 (1 book, 3 copies).	**48240140**

Volume Number	Citation	MRID Number
43	Kruedewagen, E., 20t0, Soluble Surface Content of Flumethrin and Imidacloprid of a Collar Containing 10% Imidacloprid plus 4.5% Flumethrin After Beeing Worn by Cats for Different Time Periods, 35118 (1 book, 3 copies).	**48240141**

Company Official: Douglas A. Spilker, Ph.D., Manager
EPA Regulatory Affairs

Company Name: Bayer HealthCare LLC
Animal Health Division

Company Contact: Douglas A. Spilker, Ph.D.
Phone: (913) 268-2751
Fax: (913) 268-2135
Email: doug.spilker@bayer.com

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 1 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Flumethrin Active Ingredient Specific (Pages 1 – 7)						
Product Chemistry, Section 158.300						
830.1550	Product identity and Composition	48240201	11556	OWN	23979 (BR 2625)	
830.1600	Description of materials used to produce the product	48240201	11556	OWN	23979 (BR 2625)	
830.1620	Description of production process	48240201	11556	OWN	23979 (BR 2625)	
830.1650	Description of formulation process					N.A. - EP Only
830.1670	Discussion on formation of impurities	48240201	11556	OWN	23979 (BR 2625)	
830.1700	Preliminary analysis	48240201	11556	OWN	23979 (BR 2625)	
830.1750	Certified of limits	48240201	11556	OWN	23979 (BR 2625)	
830.1800	Enforcement method	48240201	11556	OWN	23979 (BR 2625)	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color	48240202	11556	OWN	23980 (BR 2624)	
830.6303	Physical state	48240202	11556	OWN	23980 (BR 2624)	
830.6304	Odor	48240202	11556	OWN	23980 (BR 2624)	
830.6313	Stability	48240202	11556	OWN	23980 (BR 2624)	
830.6314	Oxidizing / reducing action	48240202	11556	OWN	23980 (BR 2624)	
830.6315	Flammability	48240202	11556	OWN	23980 (BR 2624)	
830.6316	Explodability	48240202	11556	OWN	23980 (BR 2624)	
830.6317	Storage stability	48240202	11556	OWN	23980 (BR 2624)	
830.6319	Miscibility	48240202	11556	OWN	23980 (BR 2624)	
830.6320	Corrosion characteristics	48240202	11556	OWN	23980 (BR 2624)	
830.6321	Dielectric breakdown volt	48240202	11556	OWN	23980 (BR 2624)	
830.7000	pH	48240202	11556	OWN	23980 (BR 2624)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 2 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.7050	UV/Visible absorption	48240202	11556	OWN	23980 (BR 2624)	
830.7100	Viscosity	48240202	11556	OWN	23980 (BR 2624)	N.A. – Not a liquid
830.7200	Melting point	48240202	11556	OWN	23980 (BR 2624)	
830.7220	Boiling point	48240202	11556	OWN	23980 (BR 2624)	
830.7300	Density, bulk-density, or specific gravity	48240202	11556	OWN	23980 (BR 2624)	
830.7370	Dissociation constant in water	48240202	11556	OWN	23980 (BR 2624)	N.A. – Does not dissociate
830.7520	Particle size, fiber length, and diameter distribution	48240202	11556	OWN	23980 (BR 2624)	
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)	48240202	11556	OWN	23980 (BR 2624)	
830.7840 830.7860	Water solubility	48240202	11556	OWN	23980 (BR 2624)	
830.7950	Vapor pressure	48240202	11556	OWN	23980 (BR 2624)	
Terrestrial and aquatic non-target organisms data requirements, Section 158.630						
850.2100	Avian oral toxicity					N.A.
850.2200	Avian dietary toxicity					N.A.
850.2400	Wild mammal toxicity					N.A.
850.2300	Avian reproduction					N.A.
850.2500	Simulated or actual field testing					N.A.
850.1075	Freshwater fish toxicity					N.A.
850.1010	Acute toxicity freshwater invertebrates					N.A.
850.1025 850.1035 830.1045 830.1055 830.1075	Acute toxicity estuarine and marine organisms					N.A.
850.1300	Aquatic invertebrates life cycle (freshwater)					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 3 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
850.1350	Aquatic invertebrates life cycle (saltwater)					N.A.
850.1400	Fish early-life stage (freshwater)					N.A.
850.1400	Fish early-life stage (saltwater)					N.A.
850.1500	Fish life cycle					N.A.
850.1710 850.1730 850.1850	Aquatic organisms bioavailability, biomagnifications, toxicity					N.A.
850.1950	Simulated or actual field testing for aquatic organisms					N.A.
850.1735	Whole sediment: acute freshwater invertebrates					N.A.
850.1740	Whole sediment: acute marine invertebrates					N.A.
850.3020	Honey bee acute contact toxicity					N.A.
850.3030	Honey bee toxicity of residues on foliage					N.A.
850.3040	Field testing for pollinators					N.A.
Toxicology, Section 158.500						
870.1100	Acute oral toxicity – rat	48240203	11556	OWN	76064 (ID 23940)	
		48240204	11556	OWN	14838	Supplemental
		48240205	11556	OWN	18186	Supplemental
870.1200	Acute dermal toxicity	48240206	11556	OWN	76065 (ID 23941)	
		48240207	11556	OWN	14837	Supplemental
870.1300	Acute inhalation toxicity – rat	48240208	11556	OWN	16302	
		48240209	11556	OWN	17815	Pilot study
		48240210	11556	OWN	17817	Pilot study

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 4 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.2400	Primary eye irritation – rabbit	48240211	11556	OWN	33853	Waiver request
		48240212	11556	OWN	14967	Supplemental Study
870.2500	Primary dermal irritation	48240213	11556	OWN	76066 (ID 23942)	
870.2600	Dermal sensitization	48240214	11556	OWN	14561	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate
870.6200	Acute neurotoxicity - rat	48240215	11556	OWN	201861 (ID 32545)	N.R. – Not an organophosphate
870.3100	90-day oral - rodent					No oral exposure
870.3150	90-day feeding - non-rodent					N.R. – Nonfood use
870.3200	21-day dermal - rabbit/rat					N.R. – Nonfood use
870.3250	90-day dermal toxicity	48240216	11556	OWN	32570	
		48240217	11556	OWN	30932	Pilot study for 32570
		48240218	11556	OWN	30931	Pilot study for 32570 and 30932
870.3465	90-day inhalation	48240219	11556	OWN	18177	
870.6100	28-day delayed neurotoxicity - hen					N.R. – Not an organophosphate
870.6200	90-day neurotoxicity - rat	48240220	11556	OWN	201706 (ID 32054)	
870.4100	Chronic oral toxicity - rodent	48240221	11556	OWN	19360	Listed as study type 870.4300 (combined)
		48240222	11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – rat	48240221	11556	OWN	19360	Listed as study type 870.4300 (combined)
		48240222	11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – mouse	48240223	11556	OWN	19383	See protocol discussion
		48240224	11556	OWN	18255	Pilot study for ID 19383
870.3700	Developmental toxicity - rat	48240225	11556	OWN	18968	
870.3700	Developmental toxicity – rabbit	48240226	11556	OWN	35286	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 5 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.3800	Reproduction and fertility effects	48240227	11556	OWN	32775	
		48240228	11556	OWN	13252	Pilot study for 32775
		48240229	11556	OWN	30322	Pilot study for 32775
		48240230	11556	OWN	30686	Pilot study for 32775
		48240231	11556	OWN	30517	Supplement to 30686
870.6300	Developmental neurotoxicity	48240232	11556	OWN	201747 (ID 32365)	
870.5100	Bacterial reverse mulation assay	48240233	11556	OWN	14173	
		48240234	11556	OWN	14174	
		48240235	11556	OWN	30687	
870.5300 870.5375	*In vitro* mammalian cell assay	48240236	11556	OWN	15461	
		48240237	11556	OWN	31492	
		48240238	11556	OWN	74691 (ID 16145)	
		48240239	11556	OWN	31489	
870.5385 870.5395	*In vitro* cytogenetics	48240240	11556	OWN	30951	
		48240241	11556	OWN	15198	
870.5550	Unscheduled DNA Synthesis	48240242	11556	OWN	14867	
870.7485	Metabolism and pharmacokinetics	48240243	11556	OWN	14368	
		48240244	11556	OWN	22813	
		48240245	11556	OWN	30971	
		48240246	11556	OWN	15839	Cattle – Supplemental Study
		48240247	11556	OWN	22818	Sheep – Supplemental Study
		48240248	11556	OWN	22819	Sheep – Supplemental Study
		48240249	11556	OWN	15987	Cattle – Supplemental Study
870.7200	Companion animal safety					N.A. for EP Only
870.7600	Dermal penetration					N.R. – See Risk Assessment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	EPA Reg No./File Symbol: 11556-RLL	Page 6 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	Product: *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	Ingredient: Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.7800	Immunotoxicity	48240250	11556	OWN	35217	
875.2400	Post-Application Exposure (Dermal)					N.A. EP Only
None	1998 EMEA Summary/Overview on Flumethtrin	48240251	11556	OWN	35038	Requested by Agency in Pre-Reg Meeting of 11/11/06
Environmental Fate, Section 158.1300						
835.2120	Hydrolysis					N.A.
835.2240	Photodegradation - water					N.A.
835.2410	Photodegradation - soil					N.A.
835.2370	Photodegradation - air					N.A.
835.4100	Aerobic soil metabolism					N.A.
835.4200	Anaerobic soil metabolism					N.A.
835.4300	Aerobic aquatic metabolism					N.A.
835.4400	Anaerobic aquatic metabolism					N.A.
835.1230 835.1240	Leaching / adsorption/desorption					N.A.
835.1410	Volatility - laboratory					N.A.
835.8100	Volatility - field					N.A.
835.6100	Terrestrial field dissipation					N.A.
835.6200	Aquatic (sediment)					N.A.
835.6300	Forestry					N.A.
835.6400	Combination and tank mixes					N.A.
835.7100	Ground water monitoring					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 7 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Residue Chemistry, Section 158.1410						
	Nature of residue - plants					N.A.
	Nature of residue - livestock and poultry					N.A.
	Residue analytical method - plants					N.A.
	Residue analytical method - animal					N.A.
	Storage stability					N.A.
	Magnitude of residues - meat/milk/poultry/egg					N.A.
	Magnitude of residue - crop field trials					N.A.
	Magnitude of residue - processed food/feed					N.A.
	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.
810.3300	Treatments to control pests of humans and pets					N.A. for EP Only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 8 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Imidacloprid Active Ingredient Specific (Pages 8 – 14)						
Product Chemistry, Section 158.240						
61-1	Chemical identity	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
61-2	Statement of Composition	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
		42270801	264	PER	BR 1785 (TGAI)	
61-3	Formation of impurities	42055302	264	PER	BR 1759 (TGAI)	
62-1	Preliminary analysis	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
		42270802	264	PER	BR 1786 (TGAI)	
62-2	Certification of limits	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
62-3	Analytical method	42055303	264	PER	BR 1760 (TGAI)	
		43213001	264	PER	BR 1874 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
63-1	Chemical and Physical Properties	42055304	264	PER	BR 1761 (TGAI)	
63-2	Appearance	42055304	264	PER	BR 1761 (TGAI)	
63-3	Physical state	42055304	264	PER	BR 1761 (TGAI)	
63-4	Odor	42055304	264	PER	BR 1761 (TGAI)	
63-5	Melting point	42055304	264	PER	BR 1761 (TGAI)	
63-6	Boiling point	42055304	264	PER	BR 1761(TGAI)	
63-7	Density	42055304	264	PER	BR 1761 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 9 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
63-8	Solubility	42055304	264	PER	BR 1761 (TGAI)	
63-9	Vapor pressure	42055304	264	PER	BR 1761 (TGAI)	
63-10	Dissociation constant					N.A. - Does not dissociate
63-11	Octanol / water partition	42055304	264	PER	BR 1761 (TGAI)	
63-12	pH	42055304	264	PER	BR 1761 (TGAI)	
63-13	Stability	42055304	264	PER	BR 1761 (TGAI)	
63-14	Oxidizing / reducing action					N.A. - No oxidative or reductive characteristics
63-15	Flammability	42055304	264	PER	BR 1761 (TGAI)	
63-16	Explodability	42055304	264	PER	BR 1761 (TGAI)	
63-17	Storage stability	42055304	264	PER	BR 1761 (TGAI)	
63-18	Viscosity					N.A. - Solid
63-19	Miscibility					N.A. - Solid
63-20	Corrosion characteristics	42055304	264	PER	BR 1761 (TGAI)	
63-21	Dielectric breakdown volt					N.A.- Solid
64-1	Submittal of samples				Samples available upon request	
Wildlife and Aquatic Organisms, Section 158.490						
71-1	Acute avian oral - quail/duck					N.A.
71-2(a)	Avian dietary - quail					N.A.
71-2(b)	Avian dietary - duck					N.A.
71-3	Wild mammal toxicity					N.A.
71-4(a)	Avian reproduction - quail					N.A.
71-4(b)	Avian reproduction – duck					N.A.
71-5	Simulated or actual field study					N.A.
72-1(a)	Fish toxicity - bluegill					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 10 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
72-1(b)	Fish toxicity bluegill - tep					N.A.
72-2(a)	Invertebrate toxicity - Daphnia					N.A.
72-2(b)	Invertebrate toxicity - Amphipods					N.A.
72-2(c)	Acute aquatic invertebrate toxicity - Chironomids					N.A.
72-3(a)	Estuarine / marine toxicity - fish					N.A.
72-3(b)	Estuarine / marine toxicity - mollusk					N.A.
72-3(c)	Estuarine/marine toxicity - shrimp					N.A.
72-4(a)	Early life stage - fish					N.A.
72-4(b)	Life cycle invertebrate					N.A.
72-7	Simulated or actual field study					N.A.
None	Foliar half-life and distribution for potatoes					N.A.
None	Runoff and Erosion predictions for apple/potato/cotton					N.A.
None	Risk assessment for apple/potato/cotton					N.A.
Toxicology, Section 158.340						
81-1	Acute oral toxicity rat	42055331	264	PER	Report No. 100040 (TGAI)	
81-2	Acute dermal toxicity, rat/rabbit	42055332	264	PER	Report No. 100041 (TGAI)	
81-3	Acute inhalation toxicity, rat	42055333	264	PER	Report No. 99806 (TGAI)	
		42286101	264	PER	Report No. 99806-1 (TGAI)	
81-4	Primary eye irritation - rabbit	42055334	264	PER	Report No. 99679 (TGAI)	
81-5	Primary dermal irritation - rabbit	42055335	264	PER	Report No. 99804 (TGAI)	
81-6	Dermal sensitization - guinea pig	42055336	264	PER	Report No. 99800 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 11 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
		43170301	264	PER	Report No. 106348	
		43285801	264	PER	Report No. 106348-1	
81-8(SS)	Acute neurotoxicity	42770301	264	PER	Report No. 103979	
82-1(a)	90-day feeding - rodent	42256327	264	PER	Report No. 100036	
82-1(b)	90-day feeding - non-rodent	42256328	264	PER	Report No. 100176	
		42256329	264	PER	Report No. 100688	
82-2	21-day dermal - rabbit/rat	48024009	264	PER	Report No. M-357205	
82-5(b)	90 day neurotoxicity - mammal	43286401	264	PER	Report No. 106356	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-1(a)	Chronic feeding toxicity - rodent	42256334	264	PER	Report No. 99672	
83-1(b)	Chronic feeding toxicity - non-rodent	42273002	264	PER	Report No. 100015	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-2(a)	Oncogenicity - rat	42256334	264	PER	Report No. 99672	
		42256335	264	PER	Report No. 100693	
		42256336	264	PER	Report No. 101929	
83-2(b)	Oncogenicity - mouse	42256337	264	PER	Report No. 99808	
83-3(a)	Developmental toxicity - rat	42256338	264	PER	Report No. 98571	
83-3(b)	Developmental toxicity - rabbit	42256339	264	PER	Report No. 98572	
83-4	Two generation reproduction - rat	42256340	264	PER	Report No. 100647	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 12 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
84-2(a)	Gene mutation (ames test)	42256341	264	PER	Report No. 101276	
		42256342	264	PER	Report No. 98584	
		42256343	264	PER	Report No. 98570	
84-2(b)	Structural chromosomal aberration	42256344	264	PER	Report No. 100021	
		42256345	264	PER	Report No. 99262	
		42256346	264	PER	Report No. 99257	
		42256347	264	PER	Report No. 102652	
		42256348	264	PER	Report No. 102654	
		42256349	264	PER	Report No. 102655	
84-4	Other genotoxic effects	42256350	264	PER	Report No. 99676	
		42256351	264	PER	Report No. 101275	
		42256352	264	PER	Report No. 98573	
		42256353	264	PER	Report No. 102653	
85-1	General metabolism	42256354	264	PER	Report No. 101999	
		42256355	264	PER	Report No. 87264	
		42256356	264	PER	Report No. 87265	
		42256357	264	PER	Report No. 102617	
870.7200 (86-1)	Domestic Animal Safety					N.A. for EP Only
95-9	Efficacy					N.A. for EP Only
Plant Protection, Section 158.540						
122-2	Aquatic plant growth					N.A.
123-2	Aquatic plant growth					N.A.
141-1	Honey bee acute contact					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 13 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
141-2	Honey bee residue on foliage					N.A.
Reentry Protection, Section 158.390						
230-236	Mixer/loader/applicator exposure	42256386 43790701	264 11556	PER OWN	Report No. 94273 Report No. 106743	
Environmental Fate, Section 158.290						
161-1	Hydrolysis					N.A.
161-2	Photodegradation - water					N.A.
161-3	Photodegradation - soil					N.A.
162-1	Acrobic soil metabolism					N.A.
162-2	Anerobic soil metabolism					N.A.
162-3	Anaerobic aquatic metabolism					N.A.
163-1	Leaching / adsorption/desorption					N.A.
164-1	Terrestrial field dissipation					N.A.
165-1	Confined rotationat crop					N.A.
165-2	Field rotational crop					N.A.
166-1	Ground water - small prospective					N.A.
None	Environmental fate summary					N.A.
Residue, Section 158.240						
171-4(a)	Nature of residue - plants					N.A.
171-4(b)	Nature of residue - livestock and poultry					N.A.
171-4(c)	Residue analytical method - plants					N.A.
171-4(d)	Residue analytical method - animal					N.A.
171-4(e)	Storage stability					N.A.
171-4(j)	Magnitude of residues - meat/milk/poultry/egg					N.A.
171-4(k)	Magnitude of residue - crop field trials					N.A.
171-4(l)						N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 14 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Magnitude of residue - processed food/feed					
(71-4(m)	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 15 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
PNR 1427 Insecticide End-Use Product Specific (Pages 15 – 18)						
Product Chemistry, Section 158.240						
830.1550	Product identity and Composition	48240101	11556	OWN	33752	
830.1600	Description of materials used to produce the product	48240101	11556	OWN	33752	
830.1620	Description of production process	48240101	11556	OWN	33752	
830.1650	Description of formulation process	48240101	11556	OWN	33752	
830.1670	Discussion on formation of impurities	48240101	11556	OWN	33752	
830.1700	Preliminary analysis					N.A. TGAI Only
830.1750	Certified of limits	48240101	11556	OWN	33752	
830.1800	Enforcement method	48240101	11556	OWN	33752	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color	48240101	11556	OWN	33752	
830.6303	Physical state	48240101	11556	OWN	33752	
830.6304	Odor	48240101	11556	OWN	33752	
830.6313	Stability					N.A. – TGAI Only
830.6314	Oxidizing / reducing action					N.A.– EP not contain an oxidizing or reducing agent
830.6315	Flammability					N.R. – This product is not considered a combustible liquid, because the closed up flashpoint for all the ingredients is > 199°F.
830.6316	Explodability					N.R. – This product does not contain any explosive ingredients.
830.6317	Storage stability					Pending; Available 3/31/2011
830.6319	Miscibility					N.R. – This product is not an emulsifiable type

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 16 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.6320	Corrosion characteristics					Pending; Available 3/31/2011
830.6321	Dielectric breakdown volt					N.A. – Not intended use around electrical equipment
830.7000	pH					N.A. – product not soluble in water and therefore pH not required.
830.7050	UV/Visible absorption					N.A. – TGAI Only
830.7100	Viscosity					N.A. – This product is a solid and viscosity is not applicable.
830.7200	Melting point					N.A.– TGAI Only
830.7220	Boiling point					N.A. – TGAI Only
830.7300	Density, bulk-density, or specific gravity					
830.7370	Dissociation constant in water					N.A. – TGAI Only
830.7520	Particle size, fiber length, and diameter distribution					N.A. – Nonfiberous product
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)					N.A. – TGAI Only
830.7840 830.7860	Water solubility					N.A. – TGAI Only
830.7950	Vapor pressure					N.A. – TGAI Only
Toxicology, Section 158.500						
870.1100	Acute oral toxicity - rat	48240102	11556	OWN	33854	Waiver request
870.1200	Acute dermal toxicity	48240103	11556	OWN	33855	Waiver request
870.1300	Acute inhalation toxicity - rat	48240104	11556	OWN	33856	Waiver request
870.2400	Primary eye irritation – rabbit	48240105	11556	OWN	33857	Waiver request
870.2500	Primary dermal irritation	48240106	11556	OWN	33749	
870.2600	Dermal sensitization	48240107	11556	OWN	33750	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 17 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.6200	Acute neurotoxicity - rat					N.R. – Not an organophosphate
870.3100	90-day oral - rodent					N.R.
870.3200	21-day dermal - rabbit/rat					N.R. – Non-food use
870.3250	90-day dermal					N.R. – Collar not affect uptake
870.7200	Companion animal safety	48240108	11556	OWN	33800	Adult cat safety study
		48240108	11556	OWN	33826	Amendment to adult cat study 33800
		48240109	11556	OWN	33805	Adult dog safety study
		48240110	11556	OWN	33806	Puppy safety study
		48240111	11556	OWN	33824	Kitten safety study
		48240112	11556	OWN	33822	Reflector study (puppy)
		48240113	11556	OWN	33823	Reflector study (kitten)
		48240114	11556	OWN	35986	Reflector study (adult cat)
		48240115	11556	OWN	35637	Reflector Study (adult dog)
Product Performance, Section 158.400						
810.3300	Treatments to control pests of humans and pets					
		48240116	11556	OWN	33801	Fleas and ticks (dogs)
		48240117	11556	OWN	33802	Fleas and ticks (cats)
		48240118	11556	OWN	33803	Efficacy with bathing and water immersion against ticks and fleas
		48240119	11556	OWN	35630	Fleas and ticks (Ixodes ricinis] (cats)
		48240120	11556	OWN	35631	Adult and larvacidal flea control; repellency and tick control (dogs)
		48240121	11556	OWN	35635	Adult and larvacidal fleas, ticks study (cats)
		48240122	11556	OWN	35644	Field studies – fleas and ticks (cats)
		48240123	11556	OWN	35645	Field studies– fleas and ticks (dogs)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX -- CONFIDENTIAL VERSION

Date: November 3, 2010	**EPA Reg No./File Symbol:** 11556-RLL	Page 18 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 -- 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Treatments to control pests of pets (cont'd)	48240124	11556	OWN	35980	Speed of kill for fleas (cats)
		48240125	11556	OWN	35987	Speed of kill for fleas (dogs)
		48240126	11556	OWN	33464	Ixodes Bridging study
		48240127	11556	OWN	35981	Ticks [Ixodes ricinis] (cats)
		48240128	11556	OWN	35979	Ticks [Ixodes ricinis] (dogs)
		48240129	11556	OWN	35982	Repellency and control of ticks (dogs)
		48240130	11556	OWN	33467	Juvenile Ticks
		48240131	11556	OWN	33694	Lice (Trichodectes canis)
		48240132	11556	OWN	33691	Sarcoptic mange
		48240133	11556	OWN	36172	Hair clipping study -- Repellency and efficacy
		48240134	11556	OWN	15962	Hair clipping study
		48240135	11556	OWN	35642	Serum and haircoat kinetics in cats
		48240136	11556	OWN	35643	Serum and haircoat kinetics in dogs
		48240137	11556	OWN	15749	Advantage Efficacy against C. canis
Miscellaneous						
None	Benefits Document (In the Public Interest)	48240138	11556	OWN	33860	Submitted w/ Flumethrin Technical Application
None	ORE Risk Assessment	48240139	11556	OWN	33861	
None	Release Rate Compilation	48240140	11556	OWN	35992	
None	Soluble Surface Content of Collar	48240141	11556	OWN	35118	

Signature Douglas A. Spilker

Douglas A. Spilker
Manager, EPA Regulatory Affairs

8 Nov. 2010

25 Aug 11556-RLL
resubm. for
pending product
→ efficacy data

Memorandum

Date: 08 / 24 / 11

To: PM 10, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- ☑ fully accepted submission
- ☐ partially accepted submission
- ☐ rejected submission

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

August 22, 2011

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

BAYER HEALTHCARE LLC
PO.BOX : 390
SHAWNEE MISSION, KS 66201-0390

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 18-AUG-11. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

Administrative Materials

Bayer
Animal Health

Via Federal Express

September 20, 2010

U.S. Bank
Government Lockbox 979074
1005 Convention Plaza
SL-MO-C2-GL
St. Louis, MO 63197

(314) 418-4990

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Subject: U.S. Environmental Protection Agency
PRIA Registration Service Fee – New Active Ingredient
R110: Nonfood Use; Indoor
Bayer Product: **Flumethrin Technical**
Bayer Company No. 11556

Dear Sir or Madam:

Please find enclosed the appropriate PRIA Service fee for the subject application for registration of ***Flumethrin Technical*** (Bayer Reg. No. 11556-XXX) and the respective end-use product ***PNR1427 Insecticide*** being submitted to the appropriate address at the Environmental Protection Agency in Washington D.C.

If you have any questions, please do not hesitate to call (913-268-2751).

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker.b@Bayer.com

Enclosure: Check No. 2000542090 ($209,475.00)

21-Day Screen Completed by Contractor

21-Day Expires on 10-15-10

Jacket # 11556 - RLL
MRID# 482401

Content Screen: Recommended to [Pass]/Fail

86-5 Review: [Passed]/Failed/NA

Transfer This Jacket to:

STEPHEN SCHAIBLE

PM-13

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 9-24-10

Experts In-Processing Signature: MF Harrington Date 9-29-10 Fee Paid: Yes __

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 11556-RLL	EPA Receipt Date: 9-24-10

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)			X		
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A)	yes: X	no:			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes:	no:			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)					X
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)			X		
		yes	no			
	a) Selective Method (Fee category experts use)	X				
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label** (link to **http://www.epa.gov/oppfead1/labeling/lrm/**) (**Electronic labels on CD are encouraged and guidance is available**)(**link to** http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)			X		

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)	X		
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**			X
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			X
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.**			X
	a) List study (or studies) not included with application			

Comments:

REGISTRANT NOTIFIED OF 86-5 DEFICIENCIES, & CORRECTED THEM PRIOR TO CLOSE OF BUSINESS ON 10/5/10. ALL STUDIES NOW PASS 86-5 REVIEW.
~~AA~~ 10/6/10

MRID 482401

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses **even if a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

September 28, 2010

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-440307
EPA File Symbol or Registration Number: 11556-RLL
Product Name: PNR1427 INSECTICIDE
EPA Receipt Date: 24-Sep-2010
EPA Company Number: 11556
Company Name: BAYER HEALTHCARE LLC

DOUGLAS A. SPILKER, PH.D.
BAYER HEALTHCARE LLC
ANIMAL HEALTH DIVISION
PO Box 390
SHAWNEE MISSION, KS 66201-0390

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-86-5 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R110.0

NEW AI;NON-FOOD USE;INDOOR;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-9362.

Sincerely,
Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{882827F~

This package includes the following

- ◉ New Registration
- ○ Amendment

☑ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 13

Receipt No. S- 882827

EPA File Symbol/Reg. No. 11556-RLL

Pin-Punch Date: 9/24/2010

☐ This item is NOT subject to FFS action.

Action Code:

Requested: R110

Granted: R110.0

Amount Due: $ -0-

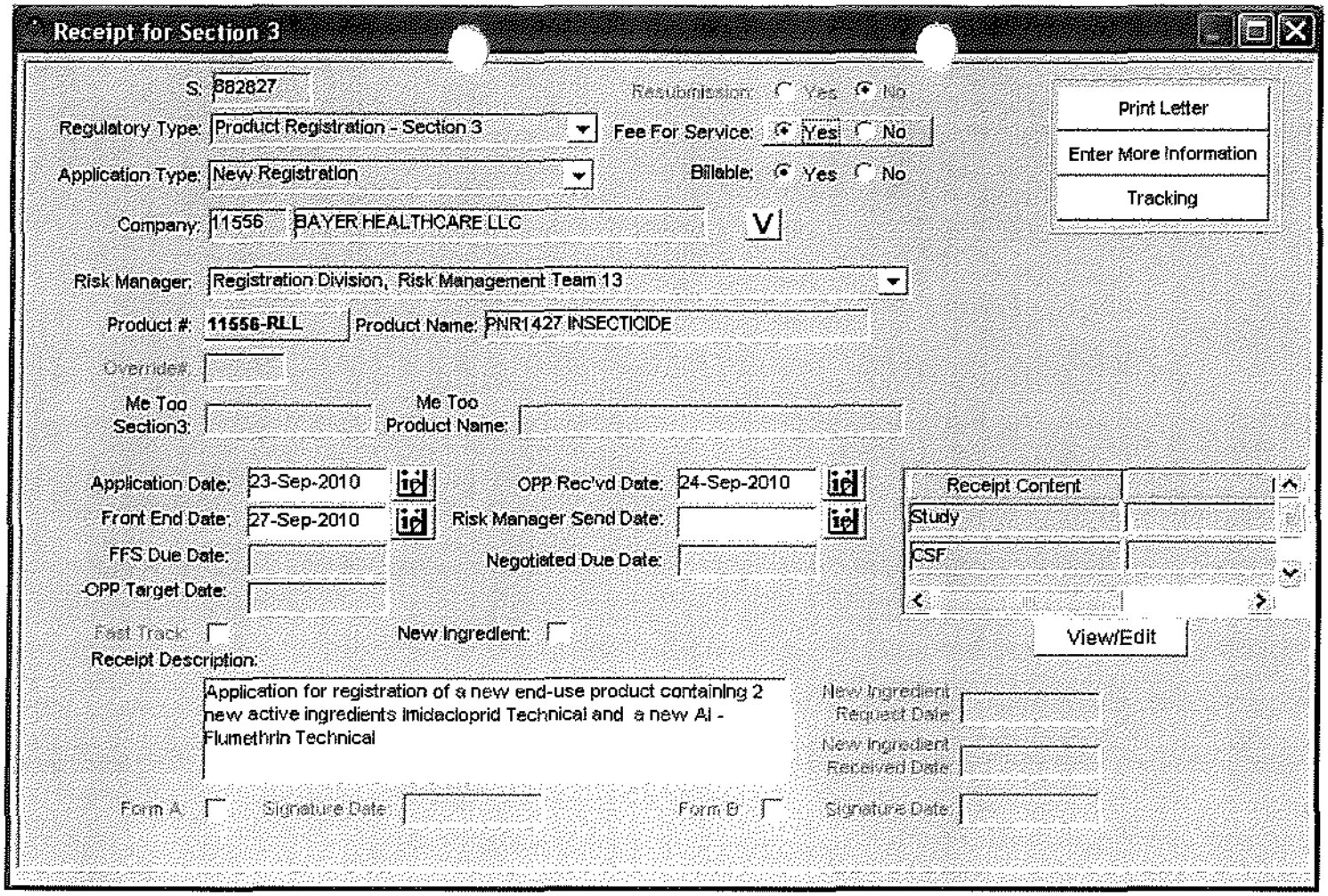
Parent/Child Decisions:

5882754/11556-RLL

☒ Inert Cleared for Intended Use ☒ Uncleared Inert in Product

Reviewer: [signature] Date: 9/28/10

Remarks:


Receipt for Section 3
S: 882827
Resubmission: Yes No
Regulatory Type: Product Registration - Section 3
Fee For Service: Yes No
Application Type: New Registration
Billable: Yes No
Print Letter
Enter More Information
Tracking
Company: 11556 BAYER HEALTHCARE LLC
Risk Manager: Registration Division, Risk Management Team 13
Product #: 11556-RLL
Product Name: PNR1427 INSECTICIDE
Override#:
Me Too Section3:
Me Too Product Name:
Application Date: 23-Sep-2010
OPP Rec'vd Date: 24-Sep-2010
Front End Date: 27-Sep-2010
Risk Manager Send Date:
FFS Due Date:
Negotiated Due Date:
OPP Target Date:
Receipt Content
Study
CSF
Fast Track:
New Ingredient:
View/Edit
Receipt Description:
Application for registration of a new end-use product containing 2 new active ingredients Imidacloprid Technical and a new AI - Flumethrin Technical
New Ingredient Request Date:
New Ingredient Received Date:
Form A:
Signature Date:
Form B:
Signature Date:

FEE FOR SERVICE

Please read instructions on reverse before c... leting form. Form Approv... OMB No. 2070-0060

Print Form

United Stotes
Environmental Protection Agency
Washington, DC 20460

[X] Registration
[ ] Amendment
[ ] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: 11556-XXX
2. EPA Product Manager: Richard Gebken
3. Proposed Classification: [X] None [ ] Restricted
4. Company/Product (Name): PNR1427 Insecticide
PM#: 10
5. Name and Address of Applicant *(Include ZIP Code)*:
Bayer HealthCare LLC, Animal Health Division
P.O. Boc 390
Shawnee Mission, K5 6620)-0390
[ ] *Check if this is a new address*
6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

[ ] Amendment - Explain below.
[ ] Resubmission in response to Agency letter dated _____
[ ] Notification - Explain below.
[ ] Final printed labels in response to Agency letter dated _____
[ ] "Me Too" Application.
[ ] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Application for registration of a new end-use product, containing 2 active ingredients – Imidacloprid Technical (EPA Reg. No. 264-755) and a new AI - Flumethrin Technical (CAS No. 69770-45-2). The application for registration of Flumethrin Technical is being submitted concurrently with this end-use application. No PRIA fee required (see attachment).

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistent Packaging	Unit Packaging	Water Soluble Peckaging	2. Type of Container
[ ] Yes* [X] No	[ ] Yes [X] No	[ ] Yes [X] No	[X] Metal [ ] Plastic [ ] Glass [X] Paper [ ] Other (Specify) _____
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Packego wgt / No. per container	

3. Location of Net Contents Information: [X] Label [ ] Container
4. Size(s) Retail Container: 0.44/1.6 oz
5. Location of Label Directions: [ ] On Label [X] On Labeling accompanying product
6. Menner in Which Label is Affixed to Product: [X] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Douglas A. Spilker, Ph.D.	Manager, EPA Reg. Affairs	(913) 268-2751

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

8. Date Application Received (Stamped)

2. Signature: Douglas A. Spilker
3. Title: Manager, EPA Regulatory Affairs
4. Typed Name: Douglas A. Spilker, Ph.D.
5. Date: 23 Sept 2010

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Application for Pesticide Registration (Continued) -
***PNR1427 Insecticide*, EPA Reg. No. 11556-XXX**

	Application Organization	Page
	Application for registration (Form 8570-1)	1
A.	PRIA Determination	2
B.	Introduction	2
C.	Product Profile	3
D.	Product Chemistry	6
E.	Acute Toxicity	7
F.	Efficacy	8
G.	Companion Animal Safety	12
H.	Occupational/Residential Exposure	14
I.	Label Development	15
J.	Ecological Effects	16
K.	Discussion of Other Requirements	16
L.	Benefits/Public Interest	16
M.	Data Compensation	16
N.	List of Attachments & Attachments 1 -7	17 -

With this application, the enclosed data and labeling, Bayer HealthCare LLC, Animal Health Division (BAH) is requesting the registration of a new end-use product, *PNR1427 Insecticide*, containing two active ingredients – the currently registered **Imidacloprid Technical** (EPA Reg. No. 264-755; CAS No. 138261-41-3) and a new active ingredient **flumethrin** (CAS No. 69770-45-2). The application for registration of *Flumethrin Technical* is being submitted concurrently with this end-use application for registration. The "specific use pattern" on domestic animals, according to the Pesticide Use Index, is determined to be Group Number 99 "Indoor – Non-Food." Several pre-registration meetings and/or teleconferences to discuss this registration action and the specific 40 CFR Part 158 requirements were held with the Agency, and will be referenced in the respective sections of this overview, and copies of referenced documents enclosed.

A. PRIA 2 DETERMINATION

The proposed *PNR1427 Insecticide* is being submitted as a formulated end-use product simultaneously with the application for registration of the new active ingredient – flumethrin technical active ingredient under the action code R110: "Nonfood use; Indoor." As described in the PRIA Decision Tree "All indoor non-food uses included in the application are covered by the base fee for the application in this category if submitted simultaneously." Therefore, since this application for the end-use product, *PNR1427 Insecticide* is being submitted simultaneously with the technical product application, there should be no additional PRIA fee for this application.

B. INTRODUCTION

The imidacloprid/flumethrin collar is a new pesticide product combining two active ingredients, 10% imidacloprid and 4.5% flumethrin in a pet collar formulation. It is intended for the prevention and treatment of ectoparasites of cats and dogs. The proposed ectoparasiticide claims include the control and treatment of ticks: American dog ticks (*Dermacentor variabilis*), Black-legged (deer) ticks (*Ixodes scapularis*), Brown dog ticks (*Rhipicephalus sanguineus*), and Lone

Star ticks (*Amblyomma americanum).* The label also includes claims for prevention and treatment of fleas (*Ctenocephalides felis, C. canis, and Pulex irritans*) on cats and dogs, and lice on dogs (*Trichodectes canis*) and for use in the treatment of Sarcoptic mange on cats and dogs. Additionally, data included in the field studies showed it to be effective against several European tick species, including *Ixodes ricinus.* All of the aforementioned pests are considered public health pests by the Agency, so efficacy data supporting these claims are enclosed with this application.

The active ingredients are released constantly from the collar in very small amounts and remain on the animal's skin and hair coat throughout an 8-month treatment period.

Two different sizes of collars have been developed. A small one (38 cm long, 12.5g/0.44 oz.) is for use on cats as well as for small dogs up to 18 lbs. (8 kg) body weight. A large collar (70 cm long, 45g/1.6 oz.) of the same formulation is for use on dogs above 18 lbs. (8 kg) body weight. The collar is fastened once around the animal's neck. Any excess length extending beyond an inch (2 cm) is directed to be cut off. After application of the collar, three optional reflector clips (contained in a separate pouch) may be fixed permanently to the collar to increase the pet's visibility in the dark.

In the United States, imidacloprid is an established insecticide and is registered by the Environmental Protection Agency in the spot-on products Advantage® Topical Solution and Advantage II for dogs and cats since 1996 and 2010, respectively. It is also used in the EPA-registered combination spot-on products with permethrin for use on dogs (K9 Advantix® and K9 Advantix II).

Flumethrin, the proposed acaricidal compound in the formulated product, is being submitted simultaneously with this application for registration as a new active ingredient by the Environmental Protection Agency. Flumethrin active ingredient is authorized in the European Union since 1986 and is used for companion and food producing animals (cats, dogs, cattle, sheep, goats, horses, and bees). Flumethrin containing products authorized in Europe are Bayticol® EC, Bayticol® Pour-on, Bayvarol® Strips and Kiltix® collar.

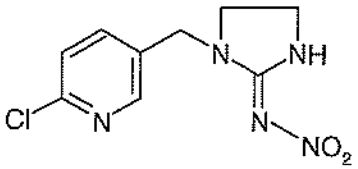
Bayer has worked to combine the excellent efficacy of imidacloprid for flea treatment and control, with flumethrin for tick prevention into an easy to administer, single administration per ectoparasitic season, low exposure, topical product with excellent pet tolerance.

C. PRODUCT PROFILE – Imidacloprid 10%/flumethrin 4.5% collar

Product:	PNR1427 Insecticide
Active Ingredients:	Imidacloprid, flumethrin
Form:	Pet collar
Strengths:	10% imidacloprid, 4.5% flumethrin
Presentation:	Package containing 1 collar packed into a pouch made of a laminated PETP/ PE foil with a separate pouch containing 3 reflectors.
Package Size:	Two different collar sizes: Small: 38 cm for cats, and dogs ≤ 18 lbs. (8kg) Large: 70 cm dogs > 18 lbs. (8kg)
Target Species:	Cats, Dogs

Imidacloprid – active ingredient

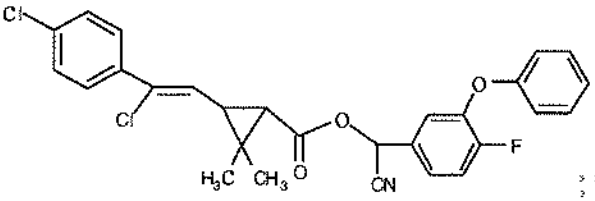
Chemical structure

INN Name	Imidacloprid	CAS No.	138261-41-3
IUPAC Names	1-(6-Chloro-3-pyridylmethyl)-N-nitro-imidazolidin-2-ylideneamine		
Laboratory Codes	NTN 33893, Bay T 7391, Confidor		
Molecular Formula	$C_9H_{10}ClN_5O_2$		
Structural Formula	 Relative molecular mass: 255.7 g/mol		
Classification	Ectoparasiticide; Agonist at the nicotinergic acetycholine receptor		

The function of imidacloprid in the present formulation for cats and dogs is as an ectoparasiticide, especially fleas. Following application of the product (collar), imidacloprid remains on the outer surface of the animal's skin and fur enabling it to come into contact with the targeted parasites and kill them. Imidacloprid interacts with the nicotinic acetylcholine receptors (nAChRs) on the post-synaptic membrane.

Flumethrin - active ingredient

Chemical structure

INN Name	Flumethrin	CAS No.	69770-45-2
IUPAC Names	(±)α-cyano-4-fluoro-3-phenoxybenzyl-3(β,4-dichlorostyryl)-2,2-dimethylcycloproprane carboxylate		
Laboratory Codes/Synonyms	Flumethrine; FLU; PNR1427; Bayticol P; Bayticol P techn.; Bayticol P active ingredient; Bayticol P Wirkstoff; BAY Vq 1950		
Empirical Formula	$C_{28}H_{22}Cl_2FNO_3$		
Structural Formula	 Relative molecular mass: 510.4 g/mol		
Classification	Ectoparasiticide; synthetic pyrethroid of the α -cyano group (Type II)		

Flumethrin is an α-cyano (type II)-pyrethroid which has been registered since 1986 in the EU for on animal use.

As the compound class is very well described and known, only a short summary for this specific compound is given: Like all α-cyano or type II pyrethroids, flumethrin acts at the sodium channels of nerves, causing the channels to remain open for longer, thus extending the period of sodium influx. This results in repeated, shorter or longer phases of nerve impulses being emitted. A secondary effect is the release of neurotransmitters, such as GABA, acetylcholine and dopamine.

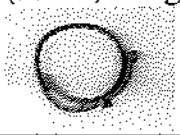
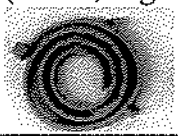
Imidacloprid and flumethrin formulated as a 10%: 4.5% collar

Characteristics of the end-use product form

The imidacloprid/flumethrin collar is a grey (alternate colors – red or yellow), odorless collar containing 10% (w/w) imidacloprid and 4.5% (w/w) flumethrin for fastening around the neck of cats and dogs. The collar provides a long term broad spectrum parasiticidal activity by combining the insecticidal active ingredient imidacloprid with the acaricidal active ingredient flumethrin. The patented Bayer collar matrix system ensures that both active ingredients are slowly and continuously released from the collar towards the animal thereby avoiding peak concentrations and ensuring that acaricidal /insecticidal concentrations of both active ingredients are present in the cat's or dog's hair coat during the entire efficacy period of 8 months. The active ingredients spread from the site of direct contact over the entire pet surface.

The collar is available in 2 different sizes, one small collar of 38 cm long (0.44 oz./12.5g) for cats, as well as for dogs up to 18 lbs. (8 kg) body weight, and one large collar of 70 cm long (1.6 oz./45 g) for dogs of more than 18 lbs. (8 kg) body weight.

The imidacloprid/flumethrin collar is intended to be potentially marketed in four (4) presentations as shown in the table below. Since the companion animal safety studies with the small collar show excellent tolerance in both dogs and cats, it may be desirable to market a single collar for optional use on either small dogs or cats.

Size of Collar	**Presentation**
Small Collar (38 cm; 12.5gm) 	• For cats • For dogs ≤ 18 lbs. (8 kg) • For cats and dogs ≤ 18 lbs. (8 kg)
Large Collar (70 cm; 45gm) 	• For dogs > 18 lbs. (8 kg)

Optional Snap-on Reflectors: In addition to the foil pouch containing the collar, the outer package will also contain 3 reflector clips in a separate pouch. As an option, these reflector clips

can be fixed permanently by the pet owner to the collar to increase the animal's visibility at night. The reflectors are regarded as a useful add-on, as they may help protect pets from, for example, being hit by cars in the dark. It has been shown that these optional reflector clips have no negative impact on companion animal safety or efficacy of the product; please refer to the Companion Animal Safety section of the application. Once the reflectors are affixed to the collar, they cannot be removed and are discarded with the expired collar.

In a pre-registration teleconference with the Agency on March 24, 2009 (see Attachment 1) the composition and potential regulatory requirements for these reflectors were discussed. Bayer proposed that no product chemistry information should be required for these reflectors. The Agency's response was that "This is acceptable to the Agency since the reflector is a device, will not be a part of the collar package (i.e. in separate bag), and contains no active ingredients." Therefore, no product chemistry or other specific information on the reflectors is enclosed with this application.

Although we have included warnings on the label that this product contains small parts which may be a potential choking hazard, these statements have been included on a voluntary basis. It is our understanding that since this product (pet collar with reflectors) will not be marketed to children as a toy, the requirements of the Consumer Product Safety Commission do not apply (Personal communication; J. Boja [CPSC] via J. Wishneff [Consumer Specialty Products Association]; Jan. 15, 2010).

D. PRODUCT CHEMISTRY

The insecticide formulation is a plastic matrix which contains the active ingredients. Three Confidential Statements of Formula (1 basic; 2 alternates) are enclosed with this application. The three versions of the Confidential Statements of Formula for the collars vary only by the different pigments they contain, and are proposed as having a gray color [redacted] red color [redacted] or yellow color [redacted] Therefore, the three respective variations of the formulation include:

Basic CSF -	Gray (PNR Basic)
Alternate 1 -	Red (PNR 1427 Alt 1 – R)
Alternate 2 -	Yellow (PNR 1427 Alt 2 – Y)

In the teleconferences with the Agency (B. Alexander and S. Mathur) on Jan. 12, 2010 and March 1, 2010, we were given guidance that: a) each formula with a different dye color must have its own CSF, and b) because of the nature of the collar, "N/A" (not applicable) should appear in the "Box 7: Bulk Density", but that the respective density information should appear in Part B of the Product Chemistry requirements. The enclosed information and reports reflect this guidance.

All of the **inert ingredients** listed on the Confidential Statements of Formula are listed in the Agency document "Inert Ingredients Permitted for Use in Nonfood Use Pesticide products, Last Updated March 28, 2010" or are proprietary blends previously evaluated and found acceptable by the Agency for use as an inert in nonfood use pesticide products. Please note that the formulation contains the proprietary blend [redacted] from [redacted] We were notified by the EPA - Inert Ingredient Assessment Branch (see Attachment 2) that "[redacted]

[redacted] Please also note, at the time of the aforementioned 09/15/2008 email, [redacted] was not approved for use in nonfood use pesticides; subsequently it was approved and now appears on "Inert Ingredients Permitted for Use in Nonfood Use Pesticide products, Last Updated March 28, 2010."

In the Pre-registration teleconference with the Agency on March 24, 2009 (see Attachment 1), Dr. Mathur gave us direction on how the flumethrin isomer ratio should be expressed on the label. The enclosed draft labeling reflects that guidance. However, direction was also given in the aforementioned teleconference that only the nominal value of the flumethrin technical needs to be reported on the Confidential Statement of Formula (CSF) for the end-use product; that is, no isomers need listing. The enclosed CSFs reflect this guidance.

Two (2) copies of each of the three (3) **Confidential Statements of Formula** (CSF) for this product are enclosed.

The **product chemistry data** to support the registration of this end-use product are found in Bayer Report ID No. 33752, entitled "Product Chemistry for M915 Insecticide (Imidacloprid + Flumethrin Collar)." Please note that the study to fulfill the requirements for a) **one-year storage stability study** (GL No. 830.6317) and b) **corrosion characteristics** (GL No. 830.6320) using the finished product is in progress (start date – 10/28/2009) and should be available for submission by 3/31/2011, well before the Agency has completed their review of this action. We request that the timing of this supplemental submission to the Agency be acceptable. As has been the Agency's previous policy, the timely submission of these data should not delay the review process.

E. ACUTE TOXICITY

The acute toxicity studies normally associated with a new formulation were not conducted because they are not practical or necessary for the pet collar product. In explanation, the physical nature of the proposed product, which is a plastic pet collar, is not a practical test article for the conduct of the "6-pack" toxicity studies (Guidelines 870.1100 – 870.2600).

BAH planned to request a waiver of 5 of the 6 studies required for the end-use product due to physical characteristics of the collar (solid plastic material). This was done previously for a similar test article - cattle ear tags. We proposed to conduct only an acute dermal irritation study with the final collar product. The studies for which a waiver was planned included: Acute oral toxicity – rat (GL No. 870.1100), acute dermal toxicity (GL No. 870.1200), acute inhalation toxicity – rat (GL No. 870.1300), primary eye irritation toxicity – rabbit (GL No. 870.2400), dermal sensitization (GL No. 870.2600).

However, as described in the meeting minutes from a teleconference with the Agency on March 30, 2009 (see Attachment 3), the Agency's response to this proposal was that this plan is reasonable (that is, to submit appropriate waiver requests) except for the omission of the dermal sensitization requirement. A dermal sensitization study should be conducted using ground collar material (may be frozen and then ground). Such a study was conducted and submitted as Bayer Report ID No. 33750.

In addition, the Agency asked in the aforementioned teleconference that we include information on the release rate of the active ingredient from the collar in our justification for the waiver of the acute oral toxicity data requirement. This information is referenced in the enclosed waiver request identified as Bayer Report ID No. 33854.

The following acute toxicity studies and/or official waiver request documents required to support the proposed product are enclosed and are titled:

EPA Guideline Number	Bayer Report ID Number	Bayer Report Title	Toxicity Category
870.1100	33854	Request for Waiver from the Requirement of Acute Oral Toxicity Study – PNR1427 Insecticide	NA
870.1200	33855	Request for Waiver from the Requirement of Acute Dermal Toxicity Study – PNR1427 Insecticide	NA
870.1300	33856	Request for Waiver from the Requirement of Acute Inhalation Toxicity Study – PNR1427 Insecticide	NA
870.2400	33857	Request for Waiver from the Requirement of Acute Eye Irritation Toxicity Study – PNR1427 Insecticide	NA
870.2500	33749	Primary Skin Irritation Study in Rabbits	IV
870.2600	33750	Dermal Sensitization Study in Guinea Pigs (Buehler Method)	Negative
		Overall Tox Category (Signal Word)	**IV Caution**

F. EFFICACY

The imidacloprid/flumethrin pet collar is designed for use on cats and dogs for the prevention and treatment of ectoparasites and remains effective for 8 months even after bathing or swimming. A pre-registration meeting was held with the Agency on September 14, 2006 (see Attachment 4) in order to obtain Agency guidance on the necessary studies required to receive acceptance of the desired performance claims. Since all of the proposed pests are considered public health pests by the Agency, efficacy data supporting these claims are enclosed with this application. Please note that some trials evaluate performance on more than one pest.

Although specific claims appear on the proposed label, in general, the main efficacy claims include:

- Treatment and prevention of flea infestations, which may also aid in the prevention of flea allergy dermatitis (FAD).
- Flea larvae in the pet's immediate surroundings are killed following contact with a treated animal.

- Kills fleas fast, based on times found in the respective residual control and "onset of efficacy" studies.
- Acaricidal and repellent efficacy against tick infestations of the brown dog tick *(Rhipicephalus sanguineus)*, Lone Star tick *(Amblyomma americanum)*, American dog tick *(Dermacentor variabilis)*, and Black-legged/Deer tick *(Ixodes scapularis)*, with efficacy against larvae, nymphs, and adult ticks. As specified in the "Product Performance Test Guidelines (OPPTS 810.3300) – Treatments to Control Pests of Humans and Pets," these data support a "general tick claim" in additional to the specific tick itemization on the product label.
- Field study reports additionally include efficacy against the European tick species (*Rhipicephalus turanicus, Ixodes ricinus,* and *Ixodes hexagonus).*
- In dogs only, treatment of lice infestations (*Trichodectes canis*)
- Aid in the treatment of sarcoptic manage
- "Waterproof" after swimming or bathing
- Duration of efficacy - 8 months

1. Efficacy against fleas

Eight (8) efficacy studies have been performed in cats and dogs to confirm the efficacy of the imidacloprid 10%/flumethrin 4.5% collar against cat fleas (*Ctenocephalides felis*) - six (6) controlled laboratory studies (3 cat/3 dog) and two controlled field studies (1 cat/1 dog). Additionally the aim of the field studies was to show the prevalence of concurrent flea and tick infestations in cats and dogs and to show the efficacy against other important flea species which are not available for laboratory studies.

Efficacy against adult cat fleas (*Ctenocephalides felis*): Six (6) laboratory efficacy studies included evaluation of the insecticidal activity of the imidacloprid/flumethrin collar against adult cat fleas (*Ctenocephalides felis*) on dogs (Bayer Report ID Nos.33801, 33803 and 35631) and on cats (33802, 35630 and 35635) as well as in two European field trials for both cats (35644) and dogs (35645). Efficacy was excellent (≥ 90%) in all studies throughout the 8-month testing period. The percentage flea control in the field studies was also excellent with most observations ≥ 95% control.

Efficacy against *Ctenocephalides canis* and *Pulex irritans*: In the dog field study (35645), 12% of the fleas identified in the baseline infestations were *C. canis*. The collar was as efficacious against these fleas as it was against *C. felis*. Further in support of this claim, imidacloprid levels have been found in the hair coat of collared dogs (see 35643) to exceed by far the imidacloprid levels in the hair of Advantage® (imidacloprid spot-on) treated dogs (15962). Since Advantage® spot-on was shown to have >95% efficacy for at least 32 days against *C. canis* (15749), this provides solid support for a *C. canis* claim for the collar.

In the same field study (ID 35645), 3.6% of the fleas identified in the baseline infestations were *P. irritans*, and the collar also was efficacious against this flea. *P. irritans* is not bred and kept under laboratory conditions, eliminating the opportunity to evaluate efficacy in a controlled laboratory study. However the field study supports efficacy against this flea.

The general flea efficacy of the collar on cats and dogs has been demonstrated in the multiple studies submitted, and is supported by the dog hair coat kinetic values discussed above. Fleas tend to not be extremely host specific, and both species can be found regularly on cats and dogs. Therefore the label claim for the control of *C. canis* and *P. irritans* on cats and dogs is supported.

Flea larvacidal efficacy: In two of the adulticidal flea efficacy studies referenced above (35631 and ID 35635), additional larval development evaluations were made to confirm the larvicidal efficacy of the product. The results of these studies confirm that imidacloprid/flumethrin collars have a marked flea larvicidal efficacy that is transferred to the animal's environment throughout the eight month efficacy period.

Onset of efficacy claims for fleas: Efficacy against fleas on both cats (35980) and dogs (35987) started immediately after treatment, resulting in 99.8 to 100% efficacy at the first 24h post-treatment count and lasted generally at >95%/24h after re-infestation for the duration of 8 months.

Re-infesting flea claims: In one cat study (33802) and one dog study (33801) additionally a "speed of kill" efficacy evaluation was conducted at day 7 post-treatment, counting fleas at 2, 6, and 12 hours after re-infestation of adult fleas. Excellent efficacy results (100%), at even the 2h count, showed that the fleas are killed extremely quickly on the pet. This suggests that flea allergy dermatitis curative efficacy can be expected to be excellent.

2. Efficacy against ticks (Cats & Dogs)

Five controlled studies on cats and dogs, plus three *in vitro* studies, were conducted to demonstrate the acaricidal and repellent efficacy of the imidacloprid 10%/flumethrin 4.5% collar against tick infestations of the brown dog tick *(Rhipicephalus sanguineus)*, Lone Star tick (*Amblyomma americanum)*, American dog tick (*Dermacentor variabilis)* and *Ixodes spp.*, with efficacy against larvae, nymphs and adult ticks.

In most studies, the curative efficacy on ticks that were already on the animal at the time of treatment (counts conducted at 48 hours post collar application) was usually below an efficacy of 90%, although clearly above 50% in the vast majority of the studies. This is not surprising as pyrethroids generally seem to have limited efficacy on partially engorged ticks that have already been on the host for several days at the time of treatment. To address this situation, information on the proposed label instructs pet owners that "Ticks already on the [(dog)(cat)] prior to treatment may not be killed immediately after collar application and may remain attached and visible. Therefore removal of ticks already on the [(dog)(cat)] at the time of application is recommended."

Therefore, only the preventive tick efficacy will be discussed here, where the animals were exposed to ticks after treatment or together with the treatment. The label reflects this use pattern.

General control of ticks (adults): In the three studies (33801, 33803 and 35631) running for the full duration of the label claim, the preventive efficacy against the brown dog tick *(Rhipicephalus sanguineus)* was above 90% for eight months. Excellent performance against this tick was also found in the European field studies (35644 and 35645). Both studies (33801 and 33803), testing the effectiveness of the collar on the American dog tick (*Dermacentor variabilis)* showed excellent performance, with efficacies above 90% for eight months. Efficacy against the

Lone Star tick (*Amblyomma americanum)* in cats was shown to be 100% throughout 8 months (33802).

Tick larvacidal/juvenile efficacy: A comparative *in-vitro* study (33467) of efficacy of a flumethrin: imidacloprid (1: 1.85) mixture was conducted against larvae, nymphs, and adults of *I. ricinus* and *R. sanguineus*, and larvae and adults of *D. reticulatus* ticks in a glass vial contact assay. Results showed the susceptibility of tick larvae and nymphs against the imidacloprid/ flumethrin mixture under evaluation is higher than that of adult ticks. Therefore, these data support the extension of the adult tick claim to "adult, nymphs, and larvae."

Onset of efficacy claims for ticks: The 6-hr efficacy evaluation (repel and/or kill) against re-infesting brown dog ticks on dogs (35631 and 35982) and *Ixodes ricinis* ticks on cats (35630, 35635 and 35981) was consistently above 97%, starting at day 2 (after the first 48h efficacy counts). The aforementioned studies, except 35981 and 35982, were conducted for 8 months.

Control of *Ixodes spp.*: The control/repellency of the black-legged/deer tick (*Ixodes scapularis*) is very important in the United States as these ticks serve as the vector for Lyme disease. As demonstrated in the aforementioned tick efficacy studies, the flumethrin component of the proposed collar is very effective against all tick species tested. Therefore, the collar could be speculated to be very effective against this tick species as well.

On March 19, 2009 in a pre-registration meeting, we notified the Agency of the short supply of black-legged/deer ticks for appropriate testing against this tick. Please note, BAH requested permission from the Agency (see Attachment 5 for correspondence) to substitute a similar tick species, *Ixodes ricinus,* for *I. scapularis.* The PERC responded (via M. Suarez, email 10/15/09) that "After discussion with the PERC, we are not inclined to consider Ix. ricinis as a substitute for Ix. scapularis. A better option would be to use wild caught Ix. scapularis from an area known to have a low incidence of Lyme disease." After pursuing the option recommended by the PERC, we received feedback from the contract research laboratories on their hesitancy to work with wild ticks due to the potential risk of exposing the test animals and laboratory workers to Lyme disease. Bayer respects their concern, and therefore this option was not possible.

As stated above, the collar has been shown to be very effective against a similar tick species (*I. ricinus*) in European testing on both cats (35630, 35635, and 35981) and dogs (35631, 35979, and 35982). Therefore, in lieu of specific testing on *I. scapularis*, we request the Agency to accept the black-legged/deer tick efficacy claim based on bridging data comparing *in vitro* susceptibility of these two tick species plus the European trials using the product against *I. ricinus*, a similar tick species.

In the bridging study, a coated glass vial contact assay (33464) was used to confirm the comparability concerning flumethrin susceptibility of two adult *Ixodes scapularis* tick strains reared in the laboratory, but originating from two different locations (Rhode Island and Connecticut) and one Laboratory strain of *Ixodes ricinus* originally found in the Berlin area in Germany. The effective concentration (EC) was evaluated by measuring tick knock down effects after 24 and 48 hours contact time. The lethal dose (LD) was evaluated by measuring tick mortality after 48 hours contact time. Inferential statistical analyses did not reveal significant differences in the susceptibility of the two Ixodes tick species towards flumethrin. Based on the review of this bridging study, comparing the susceptibility of *I. ricinus* to *I. scapularis*, in concert with the very effective results against *I. ricinus* in the European studies on both cats and

dogs, we request the Agency to reconsider the PERC decision and accept the black-legged/deer tick claims on the proposed label.

3. **"Waterproof" after swimming or bathing:** This aspect of the product usage was investigated in the already mentioned shampooing/immersion study (33803) conducted according to the protocol reviewed by the Agency (Decision No. 408242; MRID 47718601) using fleas and two species of ticks. Dogs were either shampooed with a non-medicated shampoo or immersed for five minutes in a water tank including three times of complete rinsing of the head at one week before the next scheduled flea/tick infestation. The collars were left on the test animals for the full duration of the study. Efficacy evaluation was done as usual, at 24h post re-infestation with fleas and 48h post re-infestation with ticks. The results of the study show that multiple shampooings have only a negligible effect on flea and tick efficacy, and water immersion had only a limited effect on flea efficacy, and a negligible effect on tick efficacy.

4. **Efficacy against lice (dogs only):** The efficacy against lice in dogs (*Trichodectes canis*) was documented in Bayer Report ID No. 33694. Dogs carrying an active lice infestation were treated with the imidacloprid 10%/flumethrin 4.5% collar. Efficacy was monitored at day 2 after treatment and for one consecutive month to evaluate not only the acute effect on the adult lice living on the dog, but also to monitor the effective eradication of the lice population. Efficacy against lice was 95.1% and 100% at days 2 and 7 after treatment, respectively. No lice reoccurred during the time of the study. Therefore it can be concluded that the animal was completely cured from the lice population within 48 hours.

5. **Efficacy against Sarcoptic mange:** The efficacy against Sarcoptic mange (*Sarcoptes scabiei*) was documented in a study with dogs (33691). A 100% reduction in mite numbers was observed in Sarcoptes scabiei infested dogs following treatment with the imidacloprid 10%/flumethrin 4.5% collar. A complete resolution of clinical signs (papules and crusts) associated with Sarcoptes scabiei infestations, and a >90% improvement in hair re-growth were observed in 80% of the dogs following treatment with the collar. Since the identical pest (*Sarcoptes scabiei*) infests both dogs and cats, we are proposing a general claim for PNR1427 Insecticide for the treatment of Sarcoptic mange on cats and dogs.

G. COMPANION ANIMAL SAFETY

Safety of the collar was investigated in adult cats (≥ 6 months), kittens (10-weeks), adult dogs (≥ 6 months), and puppies (7-weeks). During the safety studies, companion animals were exposed to different dose treatments including a 5x over-dosage, i.e. 5 collars were affixed around the animals' necks. Collars exhibited an excellent safety profile. There were no treatment–induced adverse systemic or local effects. Minor, transient, hair loss due to mechanical irritation from the presence of multiple collars, was observed in a few animals.

Four, separate studies were conducted to evaluate the tolerance and safety of imidacloprid 10%/flumethrin 4.5% collars in adult cats, kittens, adult dogs, and puppies:

- Both the adult cat (33800/33826) and adult dog (33805) safety studies were composed of the following four treatment groups: 0x (negative control), 1x (end-product), 5x (end-product), and 5x (placebo control). New 5x (end-product) collars were re-applied at 14-day intervals. Both studies were two-months in duration. Prior to study

initiation, the study protocols underwent Agency review: adult cats (MRID 47776601; Decision #415122), and adult dogs (MRID 47776901; Decision #415125).

- Both the kitten (33824) and puppy (33806) safety studies were composed of the following five treatment groups: 0x (negative control), 1x (end-product), 3x (end-product), 5x (end-product), and 5x (placebo control). On days 30, 90, and 150 (± 2 days), new 1x (end-product), 3x (end-product) and 5x (end-product) collars were re-applied. Both studies were six-months in duration. Prior to study initiation, the study protocols underwent Agency review: kittens (MRID 47776801; Decision #415124) and puppies (MRID 47776701; Decision #415123).

In these four safety studies, it was requested by the Agency to conduct the analysis of the collars' two active ingredients released during the studies. This information was generated and is recorded in the respective reports.

In addition to these four studies, two additional safety studies were conducted to specifically support European Union (EU) registration. As a result, the two European studies were not precisely compliant with OPPTS 870.7200. In the EU studies, no local or systemic effects, in addition to the findings already observed during the aforementioned EPA Guideline studies, were discovered. The EU studies are not enclosed but, if the Agency desires, these reports can be provided.

General safety studies in adult cats and dogs: There were no adverse treatment-induced findings or clinical effects observed in male and female cats (33800/33826), or male and female dogs (33805), continuously treated for 61 days with either zero, one, or five end-product or with five placebo collars. Mild thinning of hair, presumed to be induced by the mechanical irritation associated with multiple collars, was primarily observed in the throat area of animals wearing 5 collars (both end-product and placebo). These local changes resolved in all animals within a 7 to 35 days post study recovery period in which the 5 collars were reduced to one collar. Overall, end-product collars worn by the adult cats and dogs at 5x the recommended label dose rate for 61 consecutive days were determined to be safe.

General safety studies in kittens and puppies: No adverse treatment related findings or clinical effects were observed in male and female kittens (33824), or male or female puppies (33806) continuously treated, for 180 days with either zero, one, three, or five end-product collars or with five placebo collars. Mild hair thinning and/or hair loss, presumed to be induced by the mechanical irritation associated with multiple collars, was primarily observed in the throat and chin regions of animals wearing 5 collars (both end-product and placebo). However, these local changes self-resolved by the end of the 180-day exposure period. Overall, end-product collars worn by 10-weeks-old kittens and 7-weeks-old puppies at 1x, 3x, and 5x of the recommended label dose for 180 consecutive days were well tolerated and determined to be safe for use.

Based on the re-application of new 5x end-product collars at 30-60 day intervals throughout the kitten and puppy studies, there should be no label limitation as to when the collar can be replaced, if it were lost before its effectiveness is depleted.

Studies on potential impact of optional reflector clips on active ingredient release: Four companion animal safety studies were conducted with adult cats (35986), adult dogs (35637), puppies (33822) and kittens (33823). The studies were conducted to demonstrate the dermal

tolerance of imidacloprid 10%/flumethrin 4.5% collars when administered with or without three reflector clips. No over dosage was applied and the study duration was limited to one month. After this month, the possible adverse reactions as well as the influence of the reflectors on active ingredient release were compared between the group with and without reflectors. An important additional objective of this study was to determine if the presence of the reflectors resulted in a significant net weight loss (>10%) of the collars as compared to the collars without the reflectors (see Attachment 6).

As the standard target animal safety studies had been run without reflectors to have a "worst case scenario" with the biggest potential for maximum active ingredient release and exposure, the Agency felt it necessary for us to investigate whether the presence of the reflectors would lead to increased a.i. release and therefore increased animal exposure (See Attachment 7). The results of the studies indicate that the presence of the reflectors did not cause any adverse clinical signs nor did the presence of the reflectors and that there was no increase in the release of the active ingredients.

Companion animal tolerance and safety – conclusions: The companion animal safety studies demonstrated that the application / reapplication of end-use product to adult cats (≥ 6 months), kittens (10-weeks), adult dogs (≥ 6 months), and puppies (7-weeks) at up to 5 times the recommended unit dose applied dermally in two-monthly intervals for six months was well-tolerated with no evidence of adverse or undesirable clinical, physical (food consumption, body weight) or hematological effects.

The excellent general tolerance and safety by both cats and dogs provides a special benefit of the imidacloprid 10%/flumethrin 4.5% collar, being an ideal solution in mixed cat and dog households. As the same product can be used on both dogs and cats living closely together, they can be protected against ectoparasites, without cross-over toxicity concerns.

The safety evaluations are underlined by the results of the hair coat kinetic (35642 and 35643) studies which revealed that the matrix system releases both active ingredients slowly and continuously from the collar towards the animal thereby avoiding peak concentrations even during the first few days after treatment.

H. OCCUPATIONAL/ RESIDENTIAL EXPOSURE

An assessment (33861) of the potential exposure resulting from the use of PNR 1427 antiparasitic collars containing imidacloprid and flumethrin as the active ingredients was calculated for both handlers (applying collar) and the post application contact with treated cats, small dogs, and large dogs. The daily application rate of the active ingredients from the collars to the pets was determined based on release rate kinetic studies (35992). Hair kinetic data supported the release rate kinetics (35642 and 35643). The soluble surface data used in the analysis are also provided (35118).

The revised HED guidelines for pet exposure and risk assessments were used with the release rate data to estimate the exposure and risks to adults applying the collars and to both adults and small children contacting pets wearing the collars. Margins of Exposure (MOEs) to adults applying the collars ranged from 40,400 to 149,000. MOEs for adult post application contact with the treated pets ranged from 2,160 to 3,620. The aggregate oral and dermal MOEs for small children ranged from 1,300 to 1,630. Therefore, there should be no safety concerns for the collar

with respect to the user either during or after application of the product, provided that the product is used according to label instructions.

I. LABEL DEVELOPMENT

The collar is available in *only* 2 different sizes - small (38 cm long; 12.5g) or large (70 cm long; 45g). The collar is intended to be potentially marketed in four (4) presentations: 1) large collar for large dogs (only for dogs up to 18 lbs.), 2) small collar for cats, 3) small collar for small dogs (less than 18 lbs.) or 4) small collar for cats or small dogs. Regarding presentation #4, since the companion animal safety studies with the small collar show excellent tolerance in both cats and small dogs, it may be desirable to market a single collar for optional use on either small dogs or cats. In addition to the foil pouch containing the collar, the outer package will also contain 3 optional visibility reflector clips in a separate pouch. With all this in mind, one label is enclosed for review that encompasses the label language for all these presentations, as well as, for the reflector clips. The optional label language is designated by [brackets] or (parentheses.)

Ingredient statement: In the pre-registration teleconference with the Agency on March 24, 2009 (see Attachment 1), Dr. Mathur provided direction on how the flumethrin isomer ratio should be expressed on the label.

The precautionary label language: Because the pet collar by its very nature (solid plastic) presents unusual physical properties, not all of the acute toxicity studies normally associated with a new formulation were conducted, and waivers are being requested for those where it is impractical or impossible to conduct the respective studies. However, based on the available acute toxicity data, the over-all toxicity category for the proposed product should be Category IV (See page 8 of this application).

40 CFR § 156.64 provides guidance on the required signal words for pesticide products:
"Toxicity Category IV. A pesticide product meeting the criteria of Toxicity Category IV by all routes of exposure is not required to bear a signal word. If a signal word is used, it must be "CAUTION." Furthermore, the Label Review Manual (page 7-17) states that for products with toxicity category IV "...precautionary statements are not normally required... [but] it is recommended registrants use precautionary statements triggered by toxicity category III. Registrants may propose alternate labeling which should be reviewed by the precautionary labeling reviewers."

To that end, we have proposed CAUTION as the signal word on the subject product, and have proposed modified label language in the "HAZARDS TO HUMANS" section. We are also including First Aid statements.

Personal Protective Equipment

Neither the use pattern (residential/consumer) nor the toxicity of the product necessitate the need for any specific protective clothing.

Environmental Hazards: As described in the Label Review Manual (Page 8-1) – "1. Products which are intended for use exclusively indoors may omit the Environmental Hazards statement." Since this product is considered "Indoor – Non-Food", and the product does not have rinsate that could contaminate water (i.e., it is not a dog dip), this section is not included on the proposed label.

Storage & Disposal: Pursuant to 40 CFR § 156.140(a)(5), pet collars are exempt from the requirements of the "Container and Containment Rule." We have proposed alternative language appropriate for this type of product.

J. ECOLOGICAL EFFECTS

The specific use pattern for proposed pet collars (domestic animals), according to the Pesticide Use Index, is determined to be Group Number 99 "Indoor – Non-Food."

As described in 40 CFR §158.630 (Terrestrial and aquatic non-target organisms data requirements), there are two Conditional Requirements (CR) listed in the respective table for the "Indoor Use Pattern": 1) Freshwater fish toxicity (GL No. 850.1075) and 2) Acute toxicity freshwater invertebrates (GL No. 850.1010). However, Footnote 2 of the table that applies to both Conditional Requirements states that "The study is not required if there is no potential for environmental exposure."

Bayer discussed this with the Agency during the pre-registration meeting on 9/14/2006 (see Attachment 4) and was told that as long as we certified that the end-use product was not to be produced in the United States, then there would be "no potential for environmental exposure" and therefore these studies would not be required. Bayer HealthCare, Animal Health Division, certifies that the proposed product will not be produced in the United States. As evidenced by a statement on the proposed label, this product is "Made in Germany." Therefore, data in these areas are not enclosed with this application.

K. DISCUSSION OF OTHER REQUIREMENTS

Residue Chemistry - No residue chemistry data are provided with this application as none are necessary; this application is for a non-food use.

Child-resistant packaging - Certification that the packaging for *PNR1427 Insecticide* meets the child-resistant packaging standards in 40 CFR 157.32 is not necessary because *PNR1427 Insecticide* does not meet any of the toxicity criterion listed in 40 CFR 157.22 (a) for products requiring child resistant packaging.

L. BENEFITS/PUBLIC INTEREST

Information regarding the benefits of this new active ingredient-containing product is contained in the document entitled: "Benefits of Flumethrin Active Ingredient and the Imidacloprid/ Flumethrin Collar for Cats and Dogs (PNR1427), Bayer Report ID No. 33860" which should allow the Agency to make the determination that "...the use of the pesticide will not cause any unreasonable risk to the environment; and the use of the pesticide is in the public interest." This document is being submitted with the application for registration of *Flumethrin Technical*, being submitted simultaneously with this registration action.

M. DATA COMPENSATION

As demonstrated in the enclosed, completed "Certification with Respect to Citation of Data" (EPA Form 8570-34), we are choosing the Selective Method of Support for both the imidacloprid and flumethrin data. An appropriate data matrix listing all of the data necessary to support the registration of *PNR1427 Insecticide* is enclosed with this application.

Generic Data

Bayer CropScience is the basic registrant of imidacloprid. Accordingly, enclosed is a copy of Letter of Authorization from Bayer CropScience (EPA Company No. 264) authorizing the use of the generic imidacloprid data by the Bayer Healthcare LLC, Animal Health Division (EPA Company No. 11556).

For the flumethrin active ingredient, we are also using the selective method of support. All the data to fulfill the data requirements for flumethrin, as listed in the data matrix, are being submitted by us, Bayer HealthCare LLC, in support of the registration application of *Flumethrin Technical*, simultaneously submitted with this application.

Product Specific Data

All of the formulation specific data necessary to support the registration of *PNR1427 Insecticide* are enclosed with this application. All of these data are cited in the enclosed data matrix, and are the property of Bayer HealthCare.

N. List of Attachments

1. "Minutes of Pre Reg Meeting (03/24/09) – Collar – Product Chemistry Requirements," email (D. Spilker to B. Alexander) dated 04/13/2009, and attached minutes from Pre-registration meeting of 03/24/2009, 8pp.
2. "Inert determination – Non-food uses," email (K. Grinstead to D. Spilker) dated 9/15/2008, 3pp.
3. "Minutes of Pre-reg Meeting (03/30/09) – Collar – Acute Toxicity requirements," email (D. Spilker to B. Alexander) dated 04/13/2009, and attached minutes from Pre-registration meeting of 03/30/2009, 7pp.
4. "Minutes from US EPA & Bayer – Animal Health Division Pre-Registration Meeting for Flumethrin Technical and Flumethrin Combo Products, September 14, 2006," 5pp.
5. "Pet Collar – Deer Tick Protocol – Issue for PERC," email string including 8/14/2009, 10/7/2009 and 10/15/2009, 10pp.
6. "Domestic Animal Safety Teleconference (DRAFT minutes) – 6/4/09," and EPA response (telephone record, 6/9/2009), 4pp.
7. "Teleconference between Bayer Animal Health and EPA – Insecticide/Rodenticide Branch & Technical Review Branch, March 11, 2009; proposed Domestic Animal Safety Requirements for Flumethrin + Imidacloprid Collar, dated 5/8/2009, 4pp.

Bayer HealthCare
Animal Health

Via Federal Express

COPY

September 23, 2010

Document Processing Desk (REGFEE)
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Attention: Mr. Richard Gebken/PM10
Registration Division (7505P)

Subject: Application for Registration of a New Active Ingredient (PRIA R110): **Flumethrin Technical (CAS No. 69770-45-2)**

Application for Registration of a Combination (Flumethrin + Imidacloprid) End-Use Product: ***PNR1427 Insecticide***

Bayer HealthCare LLC
Animal Health
P.O. Box 390
Shawnee Mission, KS 66201-0390

Dear Mr. Gebken:

With this application, the enclosed data and labeling, Bayer HealthCare LLC, Animal Health Division (BAH) is requesting the registration of a new technical active ingredient – "*Flumethrin Technical*" containing **flumethrin** (CAS No. 69770-45-2). A second application for registration of *PNR1427 Insecticide* end-use product (flea and tick pet collar) is being submitted concurrently with this application for registration of the technical active ingredient. The flumethrin technical active ingredient, which is also the manufacturing-use product, is for formulation purposes ONLY into products with indoor, non-food uses. The "specific use pattern" on domestic animals, according to the Pesticide Use Index, is determined to be Group Number 99 "Indoor – Non-Food."

The proposed *Flumethrin Technical* is considered a "new" active ingredient in that it is "...not currently contained as an active ingredient in any EPA registered pesticide product." The ultimate use of this technical active ingredient is for formulation into pesticide products on pets (cats and dogs), which are considered indoor use patterns by the Agency. No flumethrin-containing end-use products are proposed that would be used on or come into contact with food and/or feed items. Therefore as described in the PRIA Decision Tree, the application for registration of this new active ingredient – *Flumethrin Technical* - falls under the action code **R110: "Nonfood use; Indoor."** Furthermore, it is our understanding that all indoor non-food use products included with this technical active

ingredient application are covered by the base fee in this category, if submitted simultaneously. The application for the end-use product, *PNR1427 Insecticide*, is being submitted simultaneously with the technical product application, and therefore there should be no additional PRIA fee for the *PNR1427 Insecticide* application.

Flumethrin, a new active ingredient, is intended as a Technical/ Manufacturing Use Product for formulating insecticides for indoor uses (on domestic animals; cats and dogs). *Flumethrin Technical* is proposed for use in combinations with other EPA-registered active ingredients (such as imidacloprid). *PNR1427 Insecticide* is a new pesticide end-use product combining two active ingredients, imidacloprid and flumethrin, in a pet collar formulation. It is intended for the prevention and treatment of public health pests, such as ticks and fleas, on kittens, cats, puppies and dogs.

The Agency is not unfamiliar with this active ingredient and end-use product, as Bayer Healthcare has had several pre-registration meetings and/or teleconferences with the Agency to discuss these registration actions and the specific 40 CFR Part 158 requirements for these products. Detailed overviews of the two actions are attached to the respective Applications for Pesticide Registration (EPA Form No. 8570-1), and the Bayer-EPA interactions will be referenced in the respective sections of these overviews, and copies of referenced documents provided. **We request that copies of the two applications with attachments be forwarded to the respective review groups, as we think this information could be quite helpful during their review processes.**

Information regarding the benefits of this new active ingredient-containing product is contained in the document entitled: "Benefits of Flumethrin Active Ingredient and the Imidacloprid/Flumethrin Collar for Cats and Dogs (PNR1427), Bayer report No. 33860," which should allow the Agency to make the determination that "...the use of the pesticide will not cause any unreasonable risk to the environment; and the use of the pesticide is in the public interest."

If you have any questions, please do not hesitate to call me at 913-268-2751.

Sincerely,

Douglas A. Spilker. Ph. D.
Manager, EPA Regulatory Affairs
Doug.Spilker@Bayer.com

Enclosures:

1. Copy of Check – Check No. 2000542090 ($209,475.00), cover letter, dated 9/20/10, and delivery confirmation, dated 9/21/2010

2. **Application for Registration – *Flumethrin Technical***

    a. Administrative Volume (Volume 1 on Transmittal Document)
        i. Cover letter (Extra Copy)
        ii. Copy of PRIA Payment (Check No. 2000542090)
        iii. Application for Registration – Flumethrin Technical (Form 8570-1), 10pp. w/ 6 attachments
        iv. Transmittal document
        v. Confidential Statement of Formula, dated 11/15/2008 (2 copies)
        vi. Certification with Respect to Citation of Data (Form 8570-34)
        vii. Data Matrix (CONFIDENTIAL) – "Flumethrin Active Ingredient Specific, dated 9/20/2010," 7pp.
        viii. Data Matrix (PUBLIC) – "Flumethrin Active Ingredient Specific, dated 9/20/2010," 7pp.
        ix. Product label, dated 9/20/2010 (3 copies)
    b. Bayer Reports – ID Nos. 23979, 23980, 23940, 14838, 18186, 23941, 14837, 16302, 17815, 17817, 33853, 14967, 76066, 14561, 32545, 32570, 30932, 30931, 18177, 201706, 19360, 15285, 19383, 18255, 18968, 35286, 32775, 13252, 30322, 30686, 30517, 32365, 14173, 14174, 30687, 15461, 31492, 74691, 31489, 30951, 15198, 14867, 14368, 22813, 30971, 15839, 22818, 22819, 15987, 35217, 35038 (3 copies each)

3. **Application for Registration – end-use product *PNR1427 Insecticide***

    a. Administrative Volume (Volume 1 on Transmittal Document)
        i. Cover letter (Extra Copy)
        ii. Application for Registration – PNR1427 Insecticide (Form 8570-1), 17pp. w/ 7 attachments
        iii. Confidential Statements of Formula (3) – Basic, Alt 1, and Alt 2, dated 8/25/2010; 2 copies each)
        iv. Transmittal Document
        v. Certification with Respect to Citation of Data (Form 8570-34)

vi. Letter of Authorization from Bayer CropScience (for imidacloprid), dated 9/7/2010
vii. Data Matrix (CONFIDENTIAL) – PNR1427 Insecticide: "Flumethrin Active Ingredient Specific (pages 1-7), Imidacloprid Active Ingredient Specific (pages 8-14), and PNR1427 Insecticide Specific (pages 15-18); dated 9/20/2010," total pages – 18
viii. Data Matrix (PUBLIC) – PNR1427 Insecticide: "Flumethrin Active Ingredient Specific (pages 1-7), Imidacloprid Active Ingredient Specific (pages 8-14), and PNR1427 Insecticide Specific (pages 15-18); dated 9/20/2010," total pages -18
ix. Product label, dated 9/20/2010 (3 copies)

b. Bayer Reports – ID Nos. 33752, 33854, 33855, 33856, 33857, 33749, 33750, 33800, 33826, 33805, 33806, 33824, 33822, 33823, 35986, 35637, 33801, 33802, 33803, 35630, 35631, 35635, 35644, 35645, 35980, 35987, 33464, 35981, 35979, 35982, 33467, 33694, 33691, 36172, 15962, 35642, 35643, 15749, 33860, 33861, 35992, 35118 (3 copies each)

TRANSMITTAL DOCUMENT

Name and Address of Submitter:	Bayer HealthCare LLC Animal Health Division Box 390 Shawnee Mission, Kansas 66201-0390
Regulatory action in support of which this package is submitted:	Application for registration of **PNR1427 Insecticide**
EPA Reg. No./File Symbol:	Company Number: 11556- XXX
Alternate Test Material Names:	N/A
Transmittal Date:	September 23, 2010
Box Count:	**19 – 24**

Volume Number	Citation	MRID Number
1	**Administrative Materials** - Cover letter (Extra Copy) - Application for Pesticide Registration (with Attachments) - Confidential Statement of Formula (2 copies) - Transmittal Document - Certification with respect to Citation of Data (8570-34) - Letter of Authorization from Bayer CropScience (imidacloprid) - Data Matrix (CONFIDENTIAL) - Data Matrix (PUBLIC) - Product Label (3 copies)	
2	Rose, J.E., 2009, Chemistry Evaluation of M915 Insecticide, 33752 (1 book, 3 copies).	
3	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Oral Toxicity Study – PNR 1427 Insecticide, 33854 (1 book, 3 copies).	
4	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Dermal Toxicity Study – PNR 1427 Insecticide, 33855 (1 book, 3 copies).	
5	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Inhalation Toxicity Study – PNR 1427 Insecticide, 33856 (1 book, 3 copies).	
6	Chopade, H., 2010, Request for Waiver from the Requirement of Acute Eye Irritation Toxicity Study – PNR 1427 Insecticide, 33857 (1 book, 3 copies).	
7	Durando, J., 2009, Primary Skin Irritation Study in Rabbits, 33749 (1 book, 3 copies).	

Volume Number	Citation	MRID Number
8	Durando, J., 2009, Dermal Sensitization Study in Guinea Pigs (Buehler Method), 33750 (1 book, 3 copies).	
9	Madsen, T.J., 2010, Safety of PNR 1427 in adult cats, 33800 (1 book, 3 copies).	
10	Madsen, T.J., 2010, Amendment to Bayer Report No.33800-Safety of PNR1427 in Adult Cats, 33826 (1 book, 3 copies).	
11	Madsen, T.J., 2010, Safety of PNR 1427 in Adult Dogs, 33805 (1 book, 3 copies).	
12	Madsen, T.J. & Chopade, H., 2010, Safety of PNR1427 in Puppies, 33806 (2 books, 3 copies).	
13	Madsen, T.J., 2010, Safety of PNR 1427 in Kittens, 33824 (2 books, 3 copies).	
14	Madsen, T.J., 2010, Safety of PNR1427 With Reflectors in Puppies, 33822 (1 book, 3 copies).	
15	Madsen, T.J., 2010, Safety of PNR1427 with Reflectors in Kittens, 33823 (1 book, 3 copies).	
t6	Delport, P.C., 2010, Target animal safety with a PNR 1427 collar with and without reflectors when applied once to adult cats, 35986 (1 book, 3 copies).	
17	Bach, T., 2010, Target Animal Safety With A 10% Imidacloprid + 4.5% Flumethrin Collar With or Without Reflector Clips Applied Once To Adult Dogs, 35637 (1 book, 3 copies).	
18	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Efficacy of PNR1427 Against Tick (Dermacentor variabilis, Rhipicephalus sanguineus) and Flea Infestations on Dogs, 33801 (1 book, 3 copies).	
19	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Efficacy of PNR1427 Against Tick (Amblyomma americanum) and Flea Infestations on Cats, 33802 (1 book, 3 copies).	
20	Everett, W.R., Davis, W.L., & Settje, T.L., 2010, Evaluation of the Effects of Shampooing or Water Immersion on the Efficacy of PNR1427 Against Flea (Ctenocephalides felis) and Tick (Dermacentor variabilis, Rhipicephalus sanguineus) Infestations on Dogs, 33803 (1 book, 3 copies).	
21	Strube, K., Stanneck, D., Schroeder, I., & Kruedewagen, E., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus) and flea (Ctenocephalides felis) infestations in cats, 35630 (1 book, 3 copies).	

Volume Number	Citation	MRID Number
22	Strube, K., Stanneck, D., Schroeder, I., & Kruedewagen, E., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus and Rhipicephalus sanguineus) and flea (Ctenocephalides felis) infestations in dogs, 35631 (1 book, 3 copies).	
23	Wolken, S., & Stanneck, D., 2010, Efficacy of a 10% imidacloprid / 4.5% flumethrin collar against experimental tick (Ixodes ricinus) and flea (Ctenocephalides felis) infestations in cats, 35635 (1 book, 3 copies).	
24	Rass, J. & Stanneck, D., 2010, Evaluation of the Efficacy, Persistency and Safety of "Imidacloprid 10%/Flumethrin 4.5% Collar" in Cats Naturally Infested with Fleas and/or Ticks in a Multi-Centric Clinical Field Study in the EU, 35644 (1 book, 3 copies).	
25	Rass, J. & Stanneck, D., 2010, Evaluation of the Efficacy, Persistency and Safety of "Imidacloprid 10%/Flumethrin 4.5% Collar" in Dogs Naturally Infested with Fleas and/or Ticks in a Multi-Centric Clinical Field Study in the EU, 35645 (1 book, 3 copies).	
26	Strube, K. & Schroeder, I., 2010, Onset of Efficacy of a 10% Imidacloprid/ 4.5% Flumethrin Collar on Cats When Experimentally Infested with the Cat Flea Ctenocephalides felis (C. felis), 35980 (1 book, 3 copies).	
27	Kok, D.J., 2010, Onset of Efficacy of an Imidacloprid/Flumethrin Collar Formulation Against Fleas (Ctenocephalides felis) on Dogs, 35987 (1 book, 3 copies).	
28	Turberg, A. & Settje, T., 2010, Comparative in-vitro study of flumethrin efficacy against two Ixodes species in a glass vial contact assay, 33464 (1 book, 3 copies).	
29	Strube, K., 2010, Onset of efficacy of a 10% Imidacloprid/ 4.5% flumethrin collar on cats when experimentally infested with *Ixodes ricinus (I. ricinus)*, 35981 (1 book, 3 copies).	
30	Ketzis, J. & Schroeder, I., 2010, A controlled, randomized study to confirm the efficacy of Imidacloprid/Flumethrin containing collars against artificially induced infestations of Ixodes ricinus on beagles, 35979 (1 book, 3 copies).	
31	Strube, K., 2010, Onset of Efficacy of a 10% Imidacloprid/ 4.5% Flumethrin Collar on Dogs when Experimentally Infested with *Ixodes ricinus* and *Rhipicephalus sanguineus*, 35982 (1 book, 3 copies).	

Volume Number	Citation	MRID Number
32	Turberg, A., 2010, Comparative in-vitro study of efficacy of a 1 : 1.85 flumethrin : imidacloprid mixture against larvae, nymphs and adults of I. ricinus and R. sanguineus and larvae and adults of D. reticulatus ticks in a glass vial contact assay, 33467 (1 book, 3 copies).	
33	Ketzis, J. & Stanneck, D., 2010, A Controlled, Randomized Study to Confirm the Efficacy of Imidacloprid/Flumethrin Containing Collars Against a Natural Infestation of Dog Lice (*Trichodectes canis*) on Mixed Bred and Purebred Dogs, 33694 (1 book, 3 copies).	
34	Fourie, J.J., 2010, Evaluation of the Efficacy of an Imidacloprid/Flumethrin Collar Formulation on Dogs with Naturally Acquired Infestations of *Sarcoptes scabiei*, 33691 (1 book, 3 copies).	
35	Kruedewagen, E., 2010, In-vitro Efficacy of Hair Coat Samples From Cats and Dogs Treated with Imidacloprid 10%/Flumethrin 4.5% Collars Against Ticks (*R. sanguineus*), 36172 (1 book, 3 copies).	
36	Gyr, P. & Hopkins, T., 1995, Residues of BAY t 7391 10% w/v Spot-on in the Coat of Dogs at Various Times After Treatment, 15962 (1 book, 3 copies).	
37	Delport, P.C., 2010, Serum and Hair Coat Kinetics of an Imidacloprid 10%/Flumethrin 4.5% Collar in Cats, 35642 (1 book, 3 copies).	
38	Delport, P.C., 2010, Serum and Hair Coat Kinetics of an Imidacloprid 10%/Flumethrin 4.5% Collar in Dogs, 35643 (1 book, 3 copies).	
39	Jacobs, D.E., 1995, Imidacloprid Spot-on 10% (BAY t 7391) for the Control of Fleas on Dogs - Clinical Field Study, 15749 (1 book, 3 copies).	
40	Spilker, D.A., & Davis, W.L., 2010, "Benefits of Flumethrin Active Ingredient and the Imidacloprid/Flumethrin Collar for Cats and Dogs (PNR1427)", 33860 (1 book, 3 copies).	
41	Lunchick, C., 2010, Occupational and Residential Exposure and Risk Assessment for PNR 1427 Dog and Cat Collars Formulated with Imidacloprid and Flumethrin, 33861 (1 book, 3 copies).	
42	Stanneck, D., 2010, Dosage of the imidacloprid 10%/flumethrin 4.5% collar and release of the active ingredients over time in cats and dogs – Review Compilation, 35992 (1 book, 3 copies).	

Volume Number	Citation	MRID Number
43	Kruedewagen, E., 2010, Soluble Surface Content of Flumethrin and Imidacloprid of a Collar Containing 10% Imidacloprid plus 4.5% Flumethrin After Beeing Worn by Cats for Different Time Periods, 35118 (1 book, 3 copies).	

Company Official: Douglas A. Spilker, Ph.D., Manager
EPA Regulatory Affairs

Company Name: Bayer HealthCare LLC
Animal Health Division

Company Contact: Douglas A. Spilker, Ph.D.
Phone: (913) 268-2751
Fax: (913) 268-2135
Email: doug.spilker@bayer.com

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Bayer HealthCare LLC, Animal Health Div., BOX 390, Shawnee Mission, KS 66201 (913-268-2751)	EPA Registration Number/File Symbol 11556-XXX
Active Ingredient(s) and/or representative test compound(s) Imidacloprid; Flumethrin	Date 23 Sept 2010
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor; Non-food Use	Product Name PNR1427 Insecticide

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

(Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements)

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Douglas A. Spilker	23 Sept 2010	Douglas A. Spilker, Mgr. EPA Reg. Affairs

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 1 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	Product: *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	Ingredient: Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Flumethrin Active Ingredient Specific (Pages 1 – 7)						
Product Chemistry, Section 158.300						
830.1550	Product identity and Composition		11556	OWN	23979 (BR 2625)	
830.1600	Description of materials used to produce the product		11556	OWN	23979 (BR 2625)	
830.1620	Description of production process		11556	OWN	23979 (BR 2625)	
830.1650	Description of formulation process					N.A. - EP Only
830.1670	Discussion on formation of impurities		11556	OWN	23979 (BR 2625)	
830.1700	Preliminary analysis		11556	OWN	23979 (BR 2625)	
830.1750	Certified of limits		11556	OWN	23979 (BR 2625)	
830.1800	Enforcement method		11556	OWN	23979 (BR 2625)	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color		11556	OWN	23980 (BR 2624)	
830.6303	Physical state		11556	OWN	23980 (BR 2624)	
830.6304	Odor		11556	OWN	23980 (BR 2624)	
830.6313	Stability		11556	OWN	23980 (BR 2624)	
830.6314	Oxidizing / reducing action		11556	OWN	23980 (BR 2624)	
830.6315	Flammability		11556	OWN	23980 (BR 2624)	
830.6316	Explodability		11556	OWN	23980 (BR 2624)	
830.6317	Storage stability		11556	OWN	23980 (BR 2624)	
830.6319	Miscibility		11556	OWN	23980 (BR 2624)	
830.6320	Corrosion characteristics		11556	OWN	23980 (BR 2624)	
830.6321	Dielectric breakdown volt		11556	OWN	23980 (BR 2624)	
830.7000	pH		11556	OWN	23980 (BR 2624)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	EPA Reg No./File Symbol: 11556-XXX	Page 2 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	Product: *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	Ingredient: Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.7050	UV/Visible absorption		11556	OWN	23980 (BR 2624)	
830.7100	Viscosity		11556	OWN	23980 (BR 2624)	N.A. – Not a liquid
830.7200	Melting point		11556	OWN	23980 (BR 2624)	
830.7220	Boiling point		11556	OWN	23980 (BR 2624)	
830.7300	Density, bulk-density, or specific gravity		11556	OWN	23980 (BR 2624)	
830.7370	Dissociation constant in water		11556	OWN	23980 (BR 2624)	N.A. – Does not dissociate
830.7520	Particle size, fiber length, and diameter distribution		11556	OWN	23980 (BR 2624)	
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)		11556	OWN	23980 (BR 2624)	
830.7840 830.7860	Water solubility		11556	OWN	23980 (BR 2624)	
830.7950	Vapor pressure		11556	OWN	23980 (BR 2624)	
Terrestrial and aquatic non-target organisms data requirements, Section 158.630						
850.2100	Avian oral toxicity					N.A.
850.2200	Avian dietary toxicity					N.A.
850.2400	Wild mammal toxicity					N.A.
850.2300	Avian reproduction					N.A.
850.2500	Simulated or actual field testing					N.A.
850.1075	Freshwater fish toxicity					N.A.
850.1010	Acute toxicity freshwater invertebrates					N.A.
850.1025 850.1035 830.1045 830.1055 830.1075	Acute toxicity estuarine and marine organisms					N.A.
850.1300	Aquatic invertebrates life cycle (freshwater)					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	EPA Reg No./File Symbol: 11556-XXX	Page 3 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	Product: *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	Ingredient: Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
850.1350	Aquatic invertebrates life cycle (saltwater)					N.A.
850.1400	Fish early-life stage (freshwater)					N.A.
850.1400	Fish early-life stage (saltwater)					N.A.
850.1500	Fish life cycle					N.A.
850.1710 850.1730 850.1850	Aquatic organisms bioavailability, biomagnifications, toxicity					N.A.
850.1950	Simulated or actual field testing for aquatic organisms					N.A.
850.1735	Whole sediment: acute freshwater invertebrates					N.A.
850.1740	Whole sediment: acute marine invertebrates					N.A.
850.3020	Honey bee acute contact toxicity					N.A.
850.3030	Honey bee toxicity of residues on foliage					N.A.
850.3040	Field testing for pollinators					N.A.
Toxicology, Section 158.500						
870.1100	Acute oral toxicity – rat		11556	OWN	76064 (ID 23940)	
			11556	OWN	14838	Supplemental
			11556	OWN	18186	Supplemental
870.1200	Acute dermal toxicity		11556	OWN	76065 (ID 23941)	
			11556	OWN	14837	Supplemental
870.1300	Acute inhalation toxicity – rat		11556	OWN	16302	
			11556	OWN	17815	Pilot study
			11556	OWN	17817	Pilot study

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 4 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.2400	Primary eye irritation – rabbit		11556	OWN	33853	Waiver request
			11556	OWN	14967	Supplemental Study
870.2500	Primary dermal irritation		11556	OWN	76066 (ID 23942)	
870.2600	Dermal sensitization		11556	OWN	14561	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate
870.6200	Acute neurotoxicity - rat		11556	OWN	201861 (ID 32545)	N.R. – Not an organophosphate
870.3100	90-day oral - rodent					No oral exposure
870.3150	90-day feeding - non-rodent					N.R. – Nonfood use
870.3200	21-day dermal - rabbit/rat					N.R. – Nonfood use
870.3250	90-day dermal toxicity		11556	OWN	32570	
			11556	OWN	30932	Pilot study for 32570
			11556	OWN	30931	Pilot study for 32570 and 30932
870.3465	90-day inhalation		11556	OWN	18177	
870.6100	28-day delayed neurotoxicity - hen					N.R. – Not an organophosphate
870.6200	90-day neurotoxicity - rat		11556	OWN	201706 (ID 32054)	
870.4100	Chronic oral toxicity - rodent		11556	OWN	19360	Listed as study type 870.4300 (combined)
			11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – rat		11556	OWN	19360	Listed as study type 870.4300 (combined)
			11556	OWN	15285	Pilot study for ID 19360
870.4200	Carcinogenicity – mouse		11556	OWN	19383	See protocol discussion
			11556	OWN	18255	Pilot study for ID 19383
870.3700	Developmental toxicity - rat		11556	OWN	18968	
870.3700	Developmental toxicity – rabbit		11556	OWN	35286	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 5 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.3800	Reproduction and fertility effects		11556	OWN	32775	
			11556	OWN	13252	Pilot study for 32775
			11556	OWN	30322	Pilot study for 32775
			11556	OWN	30686	Pilot study for 32775
			11556	OWN	30517	Supplement to 30686
870.6300	Developmental neurotoxicity		11556	OWN	201747 (ID 32365)	
870.5100	Bacterial reverse mutation assay		11556	OWN	14173	
			11556	OWN	14174	
			11556	OWN	30687	
870.5300	*In vitro* mammalian cell assay		11556	OWN	15461	
870.5375			11556	OWN	31492	
			11556	OWN	74691 (ID 16145)	
			11556	OWN	31489	
870.5385	*In vitro* cytogenetics		11556	OWN	30951	
870.5395			11556	OWN	15198	
870.5550	Unscheduled DNA Synthesis		11556	OWN	14867	
870.7485	Metabolism and pharmacokinetics		11556	OWN	14368	
			11556	OWN	22813	
			11556	OWN	30971	
			11556	OWN	15839	Cattle – Supplemental Study
			11556	OWN	22818	Sheep – Supplemental Study
			11556	OWN	22819	Sheep – Supplemental Study
			11556	OWN	15987	Cattle – Supplemental Study
870.7200	Companion animal safety					N.A. for EP Only
870.7600	Dermal penetration					N.R. – See Risk Assessment

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 6 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.7800	Immunotoxicity		11556	OWN	35217	
875.2400	Post-Application Exposure (Oermal)					N.A. EP Only
None	1998 EMEA Summary/Overview on Flumethrin		11556	OWN	35038	Requested by Agency in Pre-Reg Meeting of 11/11/06
None	1996 FAO/WHO JMPR Monograph for Flumethrin		11556	OWN	35059	Requested by Agency in Pre-Reg Meeting of 11/11/06
Environmental Fate, Section 158.1300						
835.2120	Hydrolysis					N.A.
835.2240	Photodegradation - water					N.A.
835.2410	Photodegradation - soil					N.A.
835.2370	Photodegradation - air					N.A.
835.4100	Aerobic soil metabolism					N.A.
835.4200	Anaerobic soil metabolism					N.A.
835.4300	Aerobic aquatic metabolism					N.A.
835.4400	Anaerobic aquatic metabolism					N.A.
835.1230 835.1240	Leaching / adsorption/desorption					N.A.
835.1410	Volatility - laboratory					N.A.
835.8100	Volatility - field					N.A.
835.6100	Terrestrial field dissipation					N.A.
835.6200	Aquatic (sediment)					N.A.
835.6300	Forestry					N.A.
835.6400	Combination and tank mixes					N.A.
835.7100	Ground water monitoring					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 7 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Residue Chemistry, Section 158.1410						
	Nature of residue - plants					N.A.
	Nature of residue - livestock and poultry					N.A.
	Residue analytical method - plants					N.A.
	Residue analytical method - animal					N.A.
	Storage stability					N.A.
	Magnitude of residues - meat/milk/poultry/egg					N.A.
	Magnitude of residue - crop field trials					N.A.
	Magnitude of residue - processed food/feed					N.A.
	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.
810.3300	Treatments to control pests of humans and pets					N.A. for EP Only

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 8 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-31

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Imidacloprid Active Ingredient Specific (Pages 8 – 14)						
Product Chemistry, Section 158.240						
61-1	Chemical identity	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
61-2	Statement of Composition	42055302	264	PER	BR 1759 (TGAI)	
		43306001	264	PER	BR 1879 (TGAI)	
		42270801	264	PER	BR 1785 (TGAI)	
61-3	Formation of impurities	42055302	264	PER	BR 1759 (TGAI)	
62-1	Preliminary analysis	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
		42270802	264	PER	BR 1786 (TGAI)	
62-2	Certification of limits	42055303	264	PER	BR 1760 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
62-3	Analytical method	42055303	264	PER	BR 1760 (TGAI)	
		43213001	264	PER	BR 1874 (TGAI)	
		43306002	264	PER	BR 1880 (TGAI)	
63-1	Chemical and Physical Properties	42055304	264	PER	BR 1761 (TGAI)	
63-2	Appearance	42055304	264	PER	BR 1761 (TGAI)	
63-3	Physical state	42055304	264	PER	BR 1761 (TGAI)	
63-4	Odor	42055304	264	PER	BR 1761 (TGAI)	
63-5	Melting point	42055304	264	PER	BR 1761 (TGAI)	
63-6	Boiling point	42055304	264	PER	BR 1761(TGAI)	
63-7	Density	42055304	264	PER	BR 1761 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 9 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
63-8	Solubility	42055304	264	PER	BR 1761 (TGAI)	
63-9	Vapor pressure	42055304	264	PER	BR 1761 (TGAI)	
63-10	Dissociation constant					N.A. - Does not dissociate
63-11	Octanol / water partition	42055304	264	PER	BR 1761 (TGAI)	
63-12	pH	42055304	264	PER	BR 1761 (TGAI)	
63-13	Stability	42055304	264	PER	BR 1761 (TGAI)	
63-14	Oxidizing / reducing action					N.A. - No oxidative or reductive characteristics
63-15	Flammability	42055304	264	PER	BR 1761 (TGAI)	
63-16	Explodability	42055304	264	PER	BR 1761 (TGAI)	
63-17	Storage stability	42055304	264	PER	BR 1761 (TGAI)	
63-18	Viscosity					N.A. - Solid
63-19	Miscibility					N.A. - Solid
63-20	Corrosion characteristics	42055304	264	PER	BR 1761 (TGAI)	
63-21	Dielectric breakdown volt					N.A.- Solid
64-1	Submittal of samples				Samples available upon request	
Wildlife and Aquatic Organisms, Section 158.490						
71-1	Acute avian oral - quail/duck					N.A.
71-2(a)	Avian dietary - quail					N.A.
71-2(b)	Avian dietary - duck					N.A.
71-3	Wild mammal toxicity					N.A.
71-4(a)	Avian reproduction - quail					N.A.
71-4(b)	Avian reproduction – duck					N.A.
71-5	Simulated or actual field study					N.A.
72-1(a)	Fish toxicity - bluegill					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting borden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 10 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
72-1(b)	Fish toxicity bluegill - tep					N.A.
72-2(a)	Invertebrate toxicity - Daphnia					N.A.
72-2(b)	Invertebrate toxicity - Amphipods					N.A.
72-2(c)	Acute aquatic invertebrate toxicity - Chironomids					N.A.
72-3(a)	Estuarine / marine toxicity - fish					N.A.
72-3(b)	Estuarine / marine toxicity - mollusk					N.A.
72-3(c)	Estuarine/marine toxicity - shrimp					N.A.
72-4(a)	Early life stage - fish					N.A.
72-4(b)	Life cycle invertebrate					N.A.
72-7	Simulated or actual field study					N.A.
None	Foliar half-life and distribution for potatoes					N.A.
None	Runoff and Erosion predictions for apple/potato/cotton					N.A.
None	Risk assessment for apple/potato/cotton					N.A.
Toxicology, Section 158.340						
81-1	Acute oral toxicity rat	42055331	264	PER	Report No. 100040 (TGAI)	
81-2	Acute dermal toxicity, rat/rabbit	42055332	264	PER	Report No. 100041 (TGAI)	
81-3	Acute inhalation toxicity, rat	42055333	264	PER	Report No. 99806 (TGAI)	
		42286101	264	PER	Report No. 99806-1 (TGAI)	
81-4	Primary eye irritation - rabbit	42055334	264	PER	Report No. 99679 (TGAI)	
81-5	Primary dermal irritation - rabbit	42055335	264	PER	Report No. 99804 (TGAI)	
81-6	Dermal sensitization - guinea pig	42055336	264	PER	Report No. 99800 (TGAI)	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 11 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
		43170301	264	PER	Report No. 106348	
		43285801	264	PER	Report No. 106348-1	
81-8(SS)	Acute neurotoxicity	42770301	264	PER	Report No. 103979	
82-1(a)	90-day feeding - rodent	42256327	264	PER	Report No. 100036	
82-1(b)	90-day feeding - non-rodent	42256328	264	PER	Report No. 100176	
		42256329	264	PER	Report No. 100688	
82-2	21-day dermal - rabbit/rat	48024009	264	PER	Report No. M-357205	
82-5(b)	90 day neurotoxicity - mammal	43286401	264	PER	Report No. 106356	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-1(a)	Chronic feeding toxicity - rodent	42256334	264	PER	Report No. 99672	
83-1(b)	Chronic feeding toxicity - non-rodent	42273002	264	PER	Report No. 100015	
		42256331	264	PER	Report No. 100652	
		42256332	264	PER	Report No. 101931	
		42256333	264	PER	Report No. 102658	
83-2(a)	Oncogenicity - rat	42256334	264	PER	Report No. 99672	
		42256335	264	PER	Report No. 100693	
		42256336	264	PER	Report No. 101929	
83-2(b)	Oncogenicity - mouse	42256337	264	PER	Report No. 99808	
83-3(a)	Developmental toxicity - rat	42256338	264	PER	Report No. 98571	
83-3(b)	Developmental toxicity - rabbit	42256339	264	PER	Report No. 98572	
83-4	Two generation reproduction - rat	42256340	264	PER	Report No. 100647	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 12 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
		42256341	264	PER	Report No. 101276	
		42256342	264	PER	Report No. 98584	
84-2(a)	Gene mutation (ames test)	42256343	264	PER	Report No. 98570	
		42256344	264	PER	Report No. 100021	
		42256345	264	PER	Report No. 99262	
		42256346	264	PER	Report No. 99257	
		42256347	264	PER	Report No. 102652	
		42256348	264	PER	Report No. 102654	
84-2(b)	Structural chromosomal aberration	42256349	264	PER	Report No. 102655	
		42256350	264	PER	Report No. 99676	
		42256351	264	PER	Report No. 101275	
		42256352	264	PER	Report No. 98573	
84-4	Other genotoxic effects	42256353	264	PER	Report No. 102653	
		42256354	264	PER	Report No. 101999	
		42256355	264	PER	Report No. 87264	
		42256356	264	PER	Report No. 87265	
85-1	General metabolism	42256357	264	PER	Report No. 102617	
870.7200 (86-1)	Domestic Animal Safety					N.A. for EP Only
95-9	Efficacy					N.A. for EP Only
Plant Protection, Section 158.540						
122-2	Aquatic plant growth					N.A.
123-2	Aquatic plant growth					N.A.
141-1	Honey bee acute contact					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 13 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
141-2	Honey bee residue on foliage					N.A.
Reentry Protection, Section 158.390						
230-236	Mixer/loader/applicator exposure	42256386	264	PER	Report No. 94273	
		43790701	11556	OWN	Report No. 106743	
Environmental Fate, Section 158.290						
161-1	Hydrolysis					N.A.
161-2	Photodegradation - water					N.A.
161-3	Photodegradation - soil					N.A.
162-1	Aerobic soil metabolism					N.A.
162-2	Anerobic soil metabolism					N.A.
162-3	Anaerobic aquatic metabolism					N.A.
163-1	Leaching / adsorption/desorption					N.A.
164-1	Terrestrial field dissipation					N.A.
165-1	Confined rotational crop					N.A.
165-2	Field rotational crop					N.A.
166-1	Ground water - small prospective					N.A.
None	Environmental fate summary					N.A.
Residue, Section 158.240						
171-4(a)	Nature of residue - plants					N.A.
171-4(b)	Nature of residue - livestock and poultry					N.A.
171-4(c)	Residue analytical method - plants					N.A.
171-4(d)	Residue analytical method - animal					N.A.
171-4(e)	Storage stability					N.A.
171-4(j)	Magnitude of residues - meat/milk/poultry/egg					N.A.
171-4(k)	Magnitude of residue - crop field trials					N.A.
171-4(l)						N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for infonnation, including suggestions for reducing the burden to: Director, OPPE Information Management Oivision (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 14 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Magnitude of residue - processed food/feed					
171-4(m)	Method validation/ multiresidue method					N.A.
None	Benefits Reports					N.A.
None	Dietary Analysis					N.A.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do oot send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 15 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
Product Chemistry, Section 158.240						
830.1550	Product identity and Composition		11556	OWN	33752	
830.1600	Description of materials used to produce the product		11556	OWN	33752	
830.1620	Description of production process		11556	OWN	33752	
830.1650	Description of formulation process		11556	OWN	33752	
830.1670	Discussion on formation of impurities		11556	OWN	33752	
830.1700	Preliminary analysis					N.A. TGAI Only
830.1750	Certified of limits		11556	OWN	33752	
830.1800	Enforcement method		11556	OWN	33752	
830.1900	Submittal of samples					Samples available upon request
830.6302	Color		11556	OWN	33752	
830.6303	Physical state		11556	OWN	33752	
830.6304	Odor		11556	OWN	33752	
830.6313	Stability					N.A. – TGAI Only
830.6314	Oxidizing / reducing action					N.A.– EP not contain an oxidizing or reducing agent
830.6315	Flammability					N.R. – This product is not considered a combustible liquid, because the closed up flashpnint for all the ingredients is > 199°F.
830.6316	Explodability					N.R. – This product does not contain any explosive ingredients.
830.6317	Storage stability					Pending; Available 3/31/2011
830.6319	Miscibility					N.R. – This product is not an emulsifiable type

PNR 1427 Insecticide End-Use Product Specific (Pages 15 – 18)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 16 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** ***PNR1427 Insecticide*** • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
830.6320	Corrosion characteristics					Pending; Available 3/31/2011
830.6321	Dielectric breakdown volt					N.A. – Not intended use around electrical equipment
830.7000	pH					N.A. – product not soluble in water and therefore pH not required.
830.7050	UV/Visible absorption					N.A. – TGAI Only
830.7100	Viscosity					N.A. – This product is a solid and viscosity is not applicable.
830.7200	Melting point					N.A.– TGAI Only
830.7220	Boiling point					N.A. – TGAI Only
830.7300	Density, bulk-density, or specific gravity					
830.7370	Dissociation constant in water					N.A. – TGAI Ooly
830.7520	Particle size, fiber length, and diameter distribution					N.A. – Nonfiberous product
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)					N.A. – TGAI Only
830.7840 830.7860	Water solubility					N.A. – TGAI Only
830.7950	Vapor pressure					N.A. – TGAI Only
Toxicology, Section 158.500						
870.1100	Acute oral toxicity - rat		11556	OWN	33854	Waiver request
870.1200	Acute dermal toxicity		11556	OWN	33855	Waiver request
870.1300	Acute inhalation toxicity - rat		11556	OWN	33856	Waiver request
870.2400	Primary eye irritation – rabbit		11556	OWN	33857	Waiver request
870.2500	Primary dermal irritation		11556	OWN	33749	
870.2600	Dermal sensitization		11556	OWN	33750	
870.6100	Delayed neurotoxicity (acute) - hen					N.R. – Not an organophosphate

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 17 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
870.6200	Acute neurotoxicity - rat					N.R. – Not an organophosphate
870.3100	90-day oral - rodent					N.R.
870.3200	21-day dermal - rabbit/rat					N.R. – Non-food use
870.3250	90-day dermal					N.R. – Collar not affect uptake
870.7200	Companion animal safety		11556	OWN	33800	Adult cat safety study
			11556	OWN	33826	Amendment to adult cat study 33800
			11556	OWN	33805	Adult dog safety study
			11556	OWN	33806	Puppy safety study
			11556	OWN	33824	Kitten safety study
			11556	OWN	33822	Reflector study (puppy)
			11556	OWN	33823	Reflector study (kitten)
			11556	OWN	35986	Reflector study (adult cat)
			11556	OWN	35637	Reflector Study (adult dog)
Product Performance, Section 158.400						
810.3300	Treatments to control pests of humans and pets					
			11556	OWN	33801	Fleas and ticks (dogs)
			11556	OWN	33802	Fleas and ticks (cats)
			11556	OWN	33803	Efficacy with bathing and water immersion against ticks and fleas
			11556	OWN	35630	Fleas and ticks [Ixodes ricinis] (cats)
			11556	OWN	35631	Adult and larvacidal flea control; repellency and tick control (dogs)
			11556	OWN	35635	Adult and larvacidal fleas, ticks study (cats)
			11556	OWN	35644	Field studies – fleas and ticks (cats)
			11556	OWN	35645	Field studies– fleas and ticks (dogs)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460 Form

Approved OMB No. 2070-0060

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration activities and .025 hours per response for information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the form to the address.

DATA MATRIX – CONFIDENTIAL VERSION

Date: September 23, 2010	**EPA Reg No./File Symbol:** 11556-XXX	Page 18 of 18
Bayer Health Care, LLC Animal Health Division P.O. Box 390 Shawnee Mission, KS 66201-0390	**Product:** *PNR1427 Insecticide* • Flumethrin Technical (pages 1 -7) • Imidacloprid Technical (pages 8 -14) • PNR1427 Insecticide (pages 15 – 18)	**Ingredient:** Flumethrin (CAS 69770-45-2) Imidacloprid (CAS 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Report Number	Comments
	Treatments to control pests of pets (cont'd)		11556	OWN	35980	Speed of kill for fleas (cats)
			11556	OWN	35987	Speed of kill for fleas (dogs)
			11556	OWN	33464	Ixodes Bridging study
			11556	OWN	35981	Ticks [Ixodes ricinis] (cats)
			11556	OWN	35979	Ticks [Ixodes ricinis] (dogs)
			11556	OWN	35982	Repellency and control of ticks (dogs)
			11556	OWN	33467	Juvenile Ticks
			11556	OWN	33694	Lice (Trichodectes canis)
			11556	OWN	33691	Sarcoptic mange
			11556	OWN	36172	Hair clipping study – Repellency and efficacy
			11556	OWN	15962	Hair clipping study
			11556	OWN	35642	Serum and haircoat kinetics in cats
			11556	OWN	35643	Serum and haircoat kinetics in dogs
			11556	OWN	15749	Advantage Efficacy against C. canis
Miscellaneous						
None	Benefits Document (In the Public Interest)		11556	OWN	33860	Submitted w/ Flumethrin Technical Application
None	ORE Risk Assessment		11556	OWN	33861	
None	Release Rate Compilation		11556	OWN	35992	
None	Soluble Surface Content of Collar		11556	OWN	35118	

Signature [signature] Douglas A. Spitker
Manager, EPA Regulatory Affairs
23 Sept 2010

Bayer CropScience

September 7, 2010

Document Processing Desk
Office of Pesticide Programs (7505P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, Virginia 22202-4501

Attention: Ms. Venus Eagle (PM 01, RD)

Re: Letter of Authorization: Imidacloprid
Bayer HealthCare LLC, Animal Health Division (BHC) –
Applications for Registration of PNR1427 Insecticide

Bayer CropScience
2 T.W. Alexander Drive
P. O. Box 12014
Research Triangle Park,
NC 27709
Tel: 919 549-2000

Dear Ms. Eagle,

Bayer CropScience LP (BCS) hereby authorizes the Agency to refer to and rely on any research and/or test data on our active ingredient imidacloprid (the active ingredient in ADMIRE® and PROVADO®) in support of the applications for registration of PNR1427 Insecticide submitted by Bayer HealthCare LLC, Animal Health Division (BHC), P.O. Box 390, Shawnee Mission, KS, 66201-0390.

Furthermore, BCS and BHC are wholly owned subsidiaries of Bayer Corporation. Both companies seek product registrations for products containing the active ingredient imidacloprid. Any confidential business information released by the Agency in data evaluation records or other documents for company number 264 can be disclosed without restriction to the BHC, company number 11556. In addition, the Agency is authorized to refer to any research and/or test data submitted under company number 264 in support of applications for registration from Bayer HealthCare LLC, Animal Health Division (BHC), company number 11556.

Please contact me at jamin.huang@bayercropscience.com or at 919-549-2634 if you have any questions regarding this submission.

Sincerely,

Jamin Huang, Ph.D.
Senior Regulatory Manager

CC: Doug Spilker, Ph.D., Bayer HealthCare LLC, Animal Health Division

Doug Spilker/SHAWN /AGCHEM/US/BAYER 08/14/2009 07:53 AM	To	suarez.mark@epa.gov
	cc	alexander.bewanda@epa.gov, davis.kable@epa.gov, Wendell Davis/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES
	bcc	Bruce Martin/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Anja Hoelscher/TGAHL/AH/DE/BAYER@BAYERNOTES; Jagdeep Buch/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Fiona McLellan/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES
	Subject	Pet Collar - Deer Tick Protocol - Issue for PERC

Dear Mark,
Thank you for your comments in the reviews of the 4 efficacy protocols for our pursuit of the registration of a dog/cat collar. However, we still need clarification regarding the protocol for the efficacy trial against the deer tick *(Ixodes scapularis.)* The purpose of this email is to request the Agency (via PERC) to reconsider the study requirements as outlined in your review, due to the lack of availability of *Ixodes scapularis* ticks, which is a serious problem. It will be discussed in more detail later. We feel our proposal will adequately generate the efficacy data needed to meet the performance requirement on this tick.

This is in reference to:

Product Performance/Efficacy Protocol Review
Study Title: "Efficacy of Imidacloprid + Flumethrin Collar Against Nymph and Adult *Ixodes scapularis*." MRID 47718501
Mark Suarez, Entomologist
Date: 15 May 2009
Decision#: 408237
DP Barcode: 364030
Action: R272

To summarize:

A. Bayer AH participated in Pre-reg Meeting with the Agency, March 19, 2009, to discuss efficacy requirements.

- Our understandings from the meeting are contained in the meeting minutes attached.
- We are conducting the appropriate studies to get a general tick claim.
- We understood that it would be possible to conduct an *in vitro* study to secure a "kills deer ticks (*Ixodes scapularis)*" claim, but that we should submit a protocol for review.
- The review of the protocol indicated a much more robust study than we anticipated, nor was proposed in our Pre-registration meeting.

B. Initial proposal (in the submitted protocol) for the *Ixodes scapularis* (Deer Tick) study for the Imidacloprid/Flumethrin collar:

- The study is based on a protocol method from PLRS (Corapeake, NC) for *in vitro* efficacy evaluation of deer ticks.
- The study would be conducted at BerTek (Greenbrier, AR).
- Two dogs were to be utilized in the study: One treated (receiving a collar) and one untreated.
- For each deer tick efficacy evaluation, hair is collected from multiple sites on the body

of the dogs.

- After the hair collected, it is split into six Petri dishes (six replicates per dog; the experimental unit for the study is the Petri dish).
- Deer ticks are added to the dishes (10 ticks to each dish), and efficacy evaluated in 48 hours.
- The first evaluation for efficacy was scheduled on Day 16 (tick count day), and then monthly for 8 months.

C. Based on the comments received from EPA (review and follow-up email, dated 5/29/09), we offer the following for Agency consideration :

1. Protocol Proposal

   - The following steps would be added to the study:
     a) an *in vitro* efficacy evaluation of hair from the dogs would be conducted pre-treatment (i.e. pre-qualification).
     b) the first tick efficacy evaluation would be moved to Day 7 (tick count day).
   - Consideration of the lack of tick availability:
     a) This is the limiting factor in conducting *Ixodes scapularis* (Deer Tick) studies, and would prohibit us from conducting such a robust study as you requested any time in the near future.
     b) There is only one major supplier of Ixodes ticks in the U.S. - Oklahoma State University, and the ticks from OSU are not available until mid- to late 2011 (due to demand for the ticks and the difficulty in rearing them).
     d) We have been able to secure a smaller number of ticks from the CDC to conduct the proposed *in vitro* efficacy study.

2. Alternative Bridging Proposal

   We will have available appropriate efficacy tests with the collar for the control of a similar European tick species, *Ixodes ricinus*. As an alternative to the proposed protocol, would the Agency entertain the use of these data to support a deer tick claim, if we were able to provide an *in vitro* bridging study to show that efficacy was equivalent between *Ixodes ricinus* and *Ixodes scapularis*?

   As you suggested, we are requesting that this issue be taken to the PERC for discussion and decision. We ask that you discuss both the : a) modified protocol and b) use of surrogate data with a bridging study , and provide us guidance. A prompt response would be appreciated.

   Best regards,

   Doug Spilker

   Douglas Spilker, Ph.D.
   Manager - EPA Reg. Affairs
   BAYER HEALTHCARE LLC
   ANIMAL HEALTH
   Office: +1 913-268-2751
   Mobile: +1 816-506-3102
   Fax: +1 913-268-2135
   Email: doug.spilker.b@bayer.com

   Address:
   P.O. Box 390
   Shawnee Mission, KS 66201-0390

Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

PreReg Efficacy Minutes 0309 Collar.pdf

Suarez.Mark@epamail.epa.gov
10/07/2009 03:49 PM

To Doug Spilker <doug.spilker.b@bayer.com>
cc
bcc
Subject Re: Fw: Pet Collar - Deer Tick Protocol - Issue for PERC

History: This message has been forwarded.

Doug,
The PERC discussed your tick issue today. In brief, we arrived at the following:
You must test Ix. scapularis to make claims against vectors of Lyme disease, as this is the primary vector.
If you test brown dog ticks, lone star ticks, and Ix. ricinus (with supporting bridging data for scapularis), you can make a general tick claim.
If you test on brown dog and lone star ticks, you may make claims against only those ticks.
I hope that this helps. Let me know what you want to do. I think that we still need to iron out the protocol to ensure that you have an adequate study design. But, I'll leave it to your discretion. You may feel that my previous review provided adequate direction.

Regards,
Mark

Mark E. Suarez, Entomologist
Insecticide Branch
Registration Division (7505P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

(703)305-0120
suarez.mark@epa.gov

|------------>
| From: |
|------------>

>--
--|
|Doug Spilker <doug.spilker.b@bayer.com>
|

>--
--|
|------------>
| To: |
|------------>

|Mark Suarez/DC/USEPA/US@EPA

Cc:

|BeWanda Alexander/DC/USEPA/US@EPA, Richard Gebken/DC/USEPA/US@EPA

Date:

|10/06/2009 03:51 PM

Subject:

|Fw: Pet Collar - Deer Tick Protocol - Issue for PERC

Dear Mark,
As you requested in our meeting today, please find below more information regarding the bridging study that we propose to use to support our Ixodes claim (see item 2c - "Alternative Bridging Proposal" in email attached) .

The methods of the Ixodes in vitro testing:

1) The in vitro test is a coated glass surface test

2) The testing will be conducted with flumethrin only (that is the active ingredient that kills ticks|

3) A dose response test will be conducted with both Ixodes species (Ixodes scapularis and Ixodes ricinis) to determine LD50/LD95

4) Two strains of Ixodes scapularis will be used and one strain of Ixodes ricinis

5) Each trial will have three replicates and the trial will be repeated (two trials)

6) A positive outcome will be if the LD50/LD95 for Ixodes scapularis is equal to or more sensitive to flumethrin compared to Ixodes ricinis

7) We will have in vivo studies demonstrating the efficacy of the collar against Ixodes ricinis, and this will support the efficacy against Ixodes scapularis

Please let me know if you need additional information. We look forward to a response from the PERC meeting that you have tomorrow.

Best regards,

Doug Spilker, Ph. D.
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

----- Forwarded by Doug Spilker/SHAWN/AGCHEM/US/BAYER on 10/06/2009 02:38 PM -----

To: suarez.mark@epa.gov
cc: alexander.bewanda@epa.gov, davis.kable@epa.gov, Wendell Davis/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES
Subject: Pet Collar - Deer Tick Protocol - Issue for PERC

Dear Mark,
Thank you for your comments in the reviews of the 4 efficacy protocols for our pursuit of the registration of a dog/cat collar. However, we still need clarification regarding the protocol for the efficacy trial against the deer tick (Ixodes scapularis.) The purpose of this email is to request the Agency (via PERC) to reconsider the study requirements as outlined in your review, due to the lack of availability of Ixodes scapularis ticks, which is a serious problem. It will be discussed in more detail later. We feel our proposal will adequately generate the efficacy data needed to meet the performance requirement on this tick.

This is in reference to:

Product Performance/Efficacy Protocol Review
Study Title: "Efficacy of Imidacloprid + Flumethrin Collar Against Nymph and Adult Ixodes scapularis." MRID 47718501

Mark Suarez, Entomologist
Date: 15 May 2009
Decision#: 408237
DP Barcode: 364030
Action: R272

To summarize:

A. Bayer AH participated in Pre-reg Meeting with the Agency, March 19, 2009, to discuss efficacy requirements.
Our understandings from the meeting are contained in the meeting minutes attached.
We are conducting the appropriate studies to get a general tick claim.
We understood that it would be possible to conduct an in vitro study to secure a "kills deer ticks (Ixodes scapularis)" claim, but that we should submit a protocol for review.
The review of the protocol indicated a much more robust study than we anticipated, nor was proposed in our Pre-registration meeting.

B. Initial proposal (in the submitted protocol) for the Ixodes scapularis (Deer Tick) study for the Imidacloprid/Flumethrin collar:
The study is based on a protocol method from PLRS (Corapeake, NC) for in vitro efficacy evaluation of deer ticks.
The study would be conducted at BerTek (Greenbrier, AR).
Two dogs were to be utilized in the study: One treated (receiving a collar) and one untreated.
For each deer tick efficacy evaluation, hair is collected from multiple sites on the body of the dogs.
After the hair collected, it is split into six Petri dishes (six replicates per dog; the experimental unit for the study is the Petri dish).
Deer ticks are added to the dishes (10 ticks to each dish), and efficacy evaluated in 48 hours.
The first evaluation for efficacy was scheduled on Day 16 (tick count day), and then monthly for 8 months.

C. Based on the comments received from EPA (review and follow-up email, dated 5/29/09), we offer the following for Agency consideration:

1. Protocol Proposal
The following steps would be added to the study:
a) an in vitro efficacy evaluation of hair from the dogs would be conducted pre-treatment (i.e. pre-qualification).
b) the first tick efficacy evaluation would be moved to Day 7 (tick count day).
Consideration of the lack of tick availability:
a) This is the limiting factor in conducting Ixodes scapularis (Deer Tick) studies, and would prohibit us from conducting such a robust study as you requested any time in the near future.
b) There is only one major supplier of Ixodes ticks in the U.S. - Oklahoma State University, and the ticks from OSU are not available until mid- to late 2011 (due to demand for the ticks and the difficulty in rearing them).
d) We have been able to secure a smaller number of ticks from the CDC to conduct the proposed in vitro efficacy study.
2. Alternative Bridging Proposal

We will have available appropriate efficacy tests with the collar for the control of a similar European tick species, Ixodes ricinus. As an

alternative to the proposed protocol, would the Agency entertain the use of these data to support a deer tick claim, if we were able to provide an in vitro bridging study to show that efficacy was equivalent between Ixodes ricinus and Ixodes scapularis?

As you suggested, we are requesting that this issue be taken to the PERC for discussion and decision. We ask that you discuss both the: a) modified protocol and b) use of surrogate data with a bridging study, and provide us guidance. A prompt response would be appreciated.

Best regards,

Doug Spilker

Douglas Spilker, Ph.D.
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

[attachment "PreReg Efficacy Minutes 0309 Collar.pdf" deleted by Mark Suarez/DC/USEPA/US]

Suarez.Mark@epamail.epa.gov
10/15/2009 11:37 AM

To Doug Spilker <doug.spilker.b@bayer.com>
cc Davis.Kable@epamail.epa.gov, Gebken.Richard@epamail.epa.gov
bcc
Subject Re: PERC Ixodes Discussion

History: This message has been forwarded.

Doug,
After discussion with the PERC, we are not inclined to consider Ix. ricinus as a substitute for Ix. scapularis. A better option would be to use wild caught Ix. scapularis from an area known to have a low incidence of Lyme disease.

Regards,
Mark

Mark E. Suarez, Entomologist
Insecticide Branch
Registration Division (7505P)
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460

(703)305-0120
suarez.mark@epa.gov

From: Doug Spilker <doug.spilker.b@bayer.com>

To: Mark Suarez/DC/USEPA/US@EPA

Cc: Kable Davis/DC/USEPA/US@EPA, Richard Gebken/DC/USEPA/US@EPA

Date: 10/07/2009 06:59 AM

Subject: PERC Ixodes Discussion

Mark,
Just a thought. I am in the Residential Exposure SAP in the first floor conference room until 3:00pm today (Wed.) If the PERC needs me for more information, don't hesitate to come get me.

Doug

Doug Spilker
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

Attachment 6

Doug Spilker/SHAWN/AGCHEM/US/BAYER

06/04/2009 03:45 PM

To alexander.bewanda@epa.gov

cc Dan Ciszewski/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES, Harish Chopade/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES, Jagdeep Buch/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

bcc Bruce Martin@BAYER-US-NOTES; Andrea Hentges/TGHEN/AH/DE/BAYER@BAYERNOTES; Dorothee Stanneck/VTBAT/AH/DE/BAYER@BAYERNOTES; Anja Hoelscher/TGAHL/AH/DE/BAYER@BAYERNOTES; Douglas Hutchens/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

Subject Domestic Animal Safety Teleconference (DRAFT minutes) - 6/4/09

Dear Ms. Alexander,
Thank you for your time this morning for the subject teleconference. It was agreed in the teleconference that Bayer did not need to submit formal reflector protocols for EPA review. The generation of an accurate set of minutes, reviewed and concurred by the EPA, would be sufficient. Therefore, please find attached the respective meeting minutes for the Agency's concurrence.

However, please note, there was one item that was not discussed, which we have listed in the "Variables of Interest" - Chemical analysis of the collars. It was our assumption, although not specifically stated, that chemical analysis of the collars would not be required. We would like confirmation of this, as well.

Best regards,

Doug

Doug Spilker, Ph.D.
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

EPA Mtg 2009 June 4 Flu + Imid Collar DAS.doc

Bayer HealthCare
Animal Health Division

Bayer HealthCare LLC
Animal Health Division

Date: June 4, 2009 File Reference: EPA Mtg 2009 June 4 Flu + Imid Collar DAS.doc

Subject: Teleconference between Bayer Animal Health and EPA - Insecticide/Rodenticide Branch & Technical Review Branch, June 4, 2009; Proposed Domestic Animal Safety Requirements for Flumethrin + Imidacloprid Collar

From: Douglas A. Spilker Phone: 913-268-2751

To: Ms. BeWanda Alexander EPA, Registration Branch (Team 13)

Attendees: EPA (Agency) – BeWanda Alexander, Byron Backus (TRB)
Bayer Animal Health (BAH) – Dan Ciszewski, Harish Chopade, Jagdeep Buch, and Doug Spilker

A. PURPOSE OF THE MEETING: The teleconference was requested by BAH with the topics for discussion to include:

1. Concurrence of Minutes from Our Teleconference of March 11, 2009 - We are in the process of developing the four protocols for Agency review. We would like some assurance that we have not misunderstood the Agency's recommendations on these topics/studies.

2. Effect of Reflectors on Collar AI Release Study - Due to a delay in the availability of the final reflectors, we have been notified that they will not be available before the anticipated start of the discussed Domestic Animal Safety studies. As mentioned above, we are in the process of developing the four protocols, and now realize that it will not be possible to include the respective treatments, as recommended by Dr. Backus in our teleconference of March 11th. Therefore, BAH requests guidance from EPA on how to accomplish the goal in a separate study.

B. BACKGROUND: End-product reflectors will not be available for use until early 2010. As a result, we will be unable to evaluate the effect of the reflectors on the release of the active ingredients (AIs) from the collar in conjunction with the 4 guideline (dog, cat, puppy, and kitten) safety studies. Therefore, the effect of reflectors on AI release will need to be evaluated in adjunct studies that are separate from the 4 guideline (dog, cat, puppy, and kitten) safety studies. The following represents the discussions and agreements that took place during the teleconference.

C. PROPOSAL: Adjunct studies to evaluate the effect of reflectors on AI release

- **Subgroups:** Bayer proposed that reflector studies be conducted in adult dogs and adult cats. This proposal was based on the assumption that adults, being more active than pediatrics, would generate more vigorous interaction between the reflectors and collars. EPA was willing to accept this proposal provided that our assumption was verified by chemical analysis of the collar results from the 4 guideline studies. To keep things simple, Bayer agreed to conduct separate reflector studies in healthy dogs, cats, puppies, and kittens. EPA indicated that strict age requirements, for puppies (7 weeks ± 1 day) and kittens (10 weeks ± 1 day), would not apply to the reflector studies.

- **Treatment Groups and Animals per Group:**
  Group 1 (n=2): single collar only
  Group 2 (n=2): single collar plus 3 reflectors

- **Study Duration:** 30 days

- **Variables of Interest:**
  Pre-study physical examinations
  Pre-study and post-study collar weights (x.xx gms)
  Daily clinical (systemic) observations
  Daily local observations
  Pre-study and post-study animal body weights
  Hematology and clinical chemistry would not be required.
  Chemical analysis of the collars will not be required. [PLEASE NOTE: This was not discussed in the teleconference.]

- **Proposed initiation date of the reflector studies:** QI, 2010

- **Results:** Compare the pre- and post-study collar weights between the groups. Similar differences in the pre- and post-study collar weights, in both groups, would suggest that interaction of reflectors with collars does not increase exposure to AI.

- EPA agreed that Bayer did not need to submit formal reflector protocols for EPA review. The generation of an accurate set of minutes, reviewed and concurred to by the EPA, would be sufficient.

D. Action items/EPA Guidance Regarding Proposal for Adjunct Reflector-Collar Study

1) EPA finds the conduct of a separate (adjunct) study acceptable.
2) BAH should prepare minutes for the Agency's confirmation of the understandings from this teleconference, and send via Ms. Alexander for distribution to Dr. Backus.
3) BAH will submit the four guideline study protocols for review via individual PRIA actions: a) kitten, b) adult cat, c) puppy, and d) adult dog. The PRIA review timeline is 90 days. A separate electronic submission of the WORD versions of the protocols could be helpful to the Agency during their review preparation.
4) BAH requested, if possible, that the Agency gives priority to the review of the pediatric study protocols ahead of the adult studies.

Note to Reg. Book:

Date: **June 9, 2009** (~12:30 CDT)
From: D. A. Spilker
What: Telephone record

Subject: **EPA Response to our DRAFT minutes of the Domestic Animal Safety teleconference (flumethrin + imidacloprid collar) of March 11, 2009**

BeWanda Alexander (RB) and Byron Backus (TRB) of EPA called to give us feedback on the subject meeting minutes submitted to them on May 8, 2009. They had promised to do so, in our telecom of June 4th. I suggested that Harish Chopade join the telephone call (and he did), so they could discuss any questions.

Dr. Backus said everything was okay on the minutes, and that they were a good representation of the discussion. He did, however, ask that the statistical analysis (as described in the BAH-developed attachment to the draft minutes) be altered in the proposed protocols to combine the respective two control groups to allow for more robust comparisons with the treatment groups. Harish Chopade recorded additional details.

When asked about the chemical analysis of the collars in the reflector study (see email of June 4th), he said that chemical analysis would not be needed in the reflector adjunct study unless there was a significant weight loss [i.e. in reflector treatment]. Dr. Backus said: "Just off the top of my head, I would say ≥10% weight loss would be significant."

Das 061009

Attachment 7

Bayer HealthCare
Animal Health Division

Bayer HealthCare LLC
Animal Health Division

Date: May 8, 2009 File Reference: EPA Mtg 2009 Mar 11 Flu + Imid Collar DAS.doc

Subject: Teleconference between Bayer Animal Health and EPA - Insecticide/Rodenticide Branch & Technical Review Branch, March 11, 2009; Proposed Domestic Animal Safety Requirements for Flumethrin + Imidacloprid Collar

From: Douglas A. Spilker, Ph.D. Phone: 913-268-2751

To: Ms. BeWanda Alexander EPA, Registration Branch (Team 13)

Attendees: EPA (Agency) – BeWanda Alexander, Richard Gebken (PM), Byron Backus (TRB)
Bayer Animal Health (BAH) – Dan Ciszewski, Harish Chopade, Lisa Lowseth, Bruce Martin, Mary Hunt, and Doug Spilker

A. Purpose of Meeting

The teleconference and discussion basically followed the handout order (see attached document, 4 pp.). The purpose of this meeting was to discuss with the Agency the study/data requirements to support the submission of an application for registration of a flumethrin + imidacloprid combination dog/cat flea and tick collar. Domestic Animal Safety data requirements for a spot-on formulation were previously discussed in a Pre-registration meeting with the Agency on October 11, 2006. However, due to the change in proposed formulation from a spot-on to a collar, this additional discussion was warranted due to the fact that some of the studies might not be possible due to the nature of the active ingredient and/or formulation. Please find below Bayer Animal Health's understandings from the teleconference, and the request for the Agency's concurrence on these points.

B. Study Design

Bayer indicated that the proposed studies were designed to satisfy the requirements contained in OPPTS 870.7200. However, as Bayer plans to use these safety studies to satisfy the regulatory requirements of

several different governmental agencies (EPA/USA and EMEA/EU), the Agency representatives will notice that the proposed designs sometime exceed EPA standards. The testing requirements of the EMEA, described in VICH GL 43 (Target Animal Safety for Veterinary Products), occasionally supplant the EPA guidelines and vice-versa.

Bayer provided outlines that described the design of collar safety studies in 2 distinct age/size groups of companion animals: Pediatrics (puppies & kittens / less than or equal to 8 kg body wt) and Adults (dogs & cats / greater than 8 kg body wt) [see pp 3 - 6]. During the teleconference, the outlines were addressed and discussed on a line-by-line basis. In general, the Agency accepted many of the design proposals described in Bayer's 2 study outlines. However, all recommendations, and/or revisions to the original outlines, expressed by the Agency during the teleconference, are presented below:

Pediatrics (puppies & kittens)

- Treatment Groups and Animal Numbers/Group: EPA recommended use of the limit test (deletion of the 3x group) only if we were confident that no adverse effects would develop in the 5x puppies/kittens. However, the limit design will not be used in the pediatric studies as a 3x pediatric group is an EMEA requirement.
- Chemical Analysis: Prior to use in studies, each batch of collars will have a certificate of analysis for the percentage (w/w) of imidacloprid and flumethrin contents. The proposed study designs for EPA teleconference had called for chemical analysis of the collars for residual imidacloprid and flumethrin contents after their use only in the adult dogs and cats; chemical analysis of the collars in the pediatric studies was not proposed. EPA, however, indicated that collars must be analyzed for the residual contents of the two active ingredients in both the pediatric and adult studies so that accurate exposure rates can be determined in both age groups and species. Bayer agreed to do that.
- Chemical Analysis Procedure: With regards to chemical analysis of the collars in each study, the EPA recommended weighing individual collars at the beginning and then after their use at each collar application interval. For each collar application interval in a study, collars from one male and one female showing the maximum chemical exposure [calculated as collar wt loss (g) ÷ body weight (kg)] should be analyzed for imidacloprid and flumethrin contents. As agreed to by the Agency, a batch analysis of the collar from each selected animal will be performed with the Bayer analytical method (HPLC with UV detection).

- Clinical Signs: If localized hair loss develops in some puppies and kittens, presumably due to the physical irritation associated with multiple collars (5) applied in a single layer, EPA advised us to maintain these animals following official study termination (day 180), apply one collar, and document whether or not resolution of the local irritation/hair loss occurs.

Adults (dogs & cats)

- Necropsy of study animals is required by the EPA only in the event of severe (life-threatening) reactions or death. Although not anticipated, the EMEA has indicated that the necropsy of all surviving 0x and 5x cats may become necessary if multiple non-life threatening adverse reactions develop in several adult cats. Additionally, if gross and /or microscopic lesions are identified in adults at necropsy, post-mortem examination of the kittens may also be required by EMEA. If general necropsies of the adult cats and kittens are required by EMEA, EPA requests that EMEA's decision be documented via protocol amendment.

C. Consideration of testing with Reflector Device (components = clip and reflector)

- Bayer indicated that collars may be packaged with 3 reflectors. The collar and reflectors will be in separate bags, but both bags will be contained within a single product box. Owners will have the option of affixing these reflectors to their pet's flea and tick collar.
- Bayer proposed to conduct the companion animal safety studies without reflectors in order to create conditions of maximum exposure.
- EPA proposed incorporation of an additional 1x group (n=4) to each study. For 30 days, two animals would wear a single collar without reflectors, while two different animals would each wear a single collar affixed with 3 reflectors. The collars would be weighed before application and again at the conclusion of the 30-day period. Similar pre- and post-test weights would suggest that interaction of the reflectors with the collar does not increase exposure rates.

D. Other information

During the teleconference, reference was made to the previous general pre-registration meeting on this project (March 4, 2009; D. Spilker with B. Alexander, R. Gebken and B. Backus). In the aforementioned meeting, the list of required toxicology studies [based on HED concurrence; March

14, 2007] shown did not include a chronic dog study, since this study is not required for a residential indoor use pattern. At that meeting, Dr. Backus inquired regarding the availability of a sub-chronic or chronic dog study with technical flumethrin. He inferred that these studies might be useful, if the duration of the domestic animal safety study was not adequate. In the subject teleconference, Bayer informed the Agency of the availability of two 90-day feeding studies in dogs. However, since BAH plans to conduct the domestic animal safety studies for the full duration of the label claim (6 months), this exposure duration should be adequate for the Agency to assess long-term exposure to flumethrin. However, BAH plans to submit these supplemental studies with our application for registration.

E. Action items/EPA Guidance

1) BAH should prepare minutes for the Agency's confirmation of the understandings from this teleconference, and send via Ms. Alexander for distribution within the Agency.
2) BAH will submit four protocols for review via individual PRIA actions: 1) kitten, 2) adult cat, 3) puppy, and 4) adult dog.

Attachment: "Companion Animal Safety Testing" [Document used for discussion purposes in teleconference of March 24, 2009; (4pp.)]

Das 050809

Flumethrin Technical Isomer Ratio

Flumethrin Technical is 96.2% flumethrin by weight (nominal percent of flumethrin trans-Z1 + trans-Z2 isomers). The trans-Z1 isomer is present from 54-66% and the trans-Z2 isomer is present from 34-46%. Following are some examples of how the isomer ratio could be expressed on the product label. We request the EPA's guidance on how the agency would like to see the isomer ratio expressed on the product label.

1) flumethrin 4.5%*
*isomer ratio: 60:40, trans-Z1:trans-Z2

2) flumethrin 4.5%*
*isomer ratio: 54-66% trans-Z1, 34-46% trans-Z2

3) flumethrin 4.5%*
*isomer ratio: 60% trans-Z1, 40% trans-Z2

4)[1] flumethrin 4.5%*
*isomer ratio: 2.4-3.0% trans-Z1, 1.5-2.1% trans-Z2

5)[2] flumethrin 4.5%*
*isomer ratio: 2.7% trans-Z1, 1.8% trans-Z2

6)[3] flumethrin 4.5%*
*isomer ratio: 2.7:1.8, trans-Z1:trans-Z2

[1] Absolute percent ranges of each isomer in the product based on the nominal percent flumethrin in the product.
[2] Absolute percent of each isomer in the product based on the nominal percent flumethrin in the product.
[3] Absolute ratio of trans-Z1:trans-Z2

PROTOCOL

Exhibit A

PHYSICAL AND CHEMICAL PROPERTIES TEST REQUIREMENTS

Section and Title	Test Substance End Use Product (Test Method SOP#/REF#)
63-2 (830-6302) Color:	YES (SOP126)
63-3 (830-6303) Physical State:	YES (SOP126)
63-4 (830-6304) Odor:	YES (SOP126)
63-5 (830-7200) Melting Point:	N/A* (1)
63-6 (830-7220) Boiling Point:	N/A*(1)
63-7 (830-7300) Density, bulk density, or specific gravity:	YES (SOP129)
63-8 (830-7840) (830-7860) Solubility:	N/A*(1)
63-9 (830-7950) Vapor Pressure:	N/A*(1)
63-10 (830-7370) Dissociation Constant:	N/A*(1)
63-11 (830-7550) Octanol/water partition coefficient	N/A*(1)
63-12 (830-7000) pH:	N/A*(2)
63-13 (830-6313) Stability:	N/A*(1)
63-14 (830-6314) Oxidation or reducing:	Will not act as an oxidizing or reducing agent
63-15 (830-6315) Flammability - flashpoint (combustible liquids only)	N/A*(3)
63-16 (830-6316) Explodability:	N/A*(4)
63-17 (830-6317) Storage Stability:	N/A*(5)
63-18 (830-7100) Viscosity: (Liquids Only)	N/A*(9)
63-19 (830-6319) Miscibility: (emulsifiable liquids and is to be diluted with petroleum solvent)	N/A*(6)

* N/A = Not Applicable

PROTOCOL

PHYSICAL AND CHEMICAL PROPERTIES TEST REQUIREMENTS (continued)

Section and Title	Test Substance End Use Product (Test Method SOP#/REF#)\
63-20 (830-6320) Corrosion characteristics: (when packaged in metal, plastic or paper containers)	N/A*(8)
63-21 (830-6321) Dielectric breakdown voltage: (yes if for use around electrical equipment)	N/A*(7)
61-3 (830-1670)Formation of unintentional ingredients during manufacturing	Not likely to form unintentional ingredients during manufacturing

* N/A = Not Applicable

1) Per 40 CFR 158.190 - This test is only required on Technical grade of active ingredient and not for end use product.

2) Per 40 CFR 158.190, This product is not soluble in water and pH of the test substance is not required.

3) Per 40 CFR 158.190; 63-15(a) - This product is not considered a combustible liquid, because the closed cup flashpoint for all the ingredients is greater than 199E F.

4) Per 40 CFR 158.190; 63-16(a) - This product does not contain any explosive ingredients.

5) Per 40 CFR 158.190; 63-17 - This is a study to support stability of the product in the market container. Stability is not part this study but will done under a separate study.

6) Per 40 CFR 158.190; 63-19(a) - This product is not an emulsifiable concentrate type product.

7) Per 40 CFR 158.190; 63-21(a) - This product is not intended for use around electrical equipment.

8) Per 40 CFR 158.190; 63-20 - This is a study to support corrosion of the product in the market container and not part of his study but done under a separate study.

9) Per 40 CFR 158 190, 63-18. The product is a solid and viscosity is not applicable

Attachment 2

Grinstead.Keri@epamail.epa.gov
09/15/2008 06:28 PM

To Doug Spilker <doug.spilker.b@bayer.com>
cc
bcc
Subject Re: Inert determination - Non-Food uses

History: This message has been replied to and forwarded.

Hi Doug,

[redacted]

Here are some general instructions for submitting a new nonfood inert ingredient request and supporting data/discussion to the Inert Ingredient Assessment Branch (IIAB). There is currently no fee associated with a new nonfood inert ingredient request and the review time for a complete/adequate submission is approximately 6-12 months, dependent upon how many requests are ahead of you in the queue. (Note: Submissions of new conventional product registrations or amendments are not accepted until the inert is approved)

Your submission package should include a request letter and any/all supporting data/discussion. The request letter should be used as the cover letter for the submission and needs to include (1) Subject line that reads "Request for Approval of a New Nonfood Use Inert Ingredient: [insert your chemical name and CAS Reg. No.]", (2) Summary details of your request (description, proposed use, etc.), and (3) A list of studies you are submitting with your package in support of your request.

The information typically used by the Agency to make a decision for these types of requests includes: physical/chemical properties, toxicity data (from animal studies), environmental fate and effects data, ecotoxicity data, as well as your discussion of anticipated exposure from your proposed use of this chemical and your discussion of how, based on the overall toxicity profile of the chemical, your proposed use of the chemical would be considered safe for human health and the environment.

We may also consider other publicly available information from review programs such as High Production Volume Challenge Program, IUCLID

datasets, OECD SIDS, etc., as well as other publicly available, peer-reviewed literature. Information on surrogate chemicals and structure activity relationships may also be considered.

All study data need to be included in your submission package. Please be aware that there are standard data format requirements for all study data submitted to the Agency under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA) . These requirements are outlined in (PR) Notice 86-5. For your reference, a link to this Notice is provided below. Submitted data packages that do not conform to these requirements may be returned to the submitter for necessary revision.

http://www.epa.gov/PR_Notices/pr86-5.html

Upon receipt, IIAB screens all submission packages for completeness. Only those packages deemed complete are placed in queue for IIAB review. Submissions are placed in the review queue in the order they are deemed complete. You will be notified of any deficiencies.

All submissions to IIAB need to be received and processed by our Document Processing Desk. Please use the addressing instructions below. **Please note** the address is different depending on the type of delivery service you plan to use.

Address for U.S. Post Office deliveries ONLY:

Inert Ingredient Assessment Branch/Registration Division
Office of Pesticide Programs
Document Processing Desk (Mail Code 7504P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington DC, 20460

Address for FedEx, UPS, DHL, Courier Deliveries ONLY:

Inert Ingredient Assessment Branch/Registration Division
Office of Pesticide Programs
Document Processing Desk, 4th Floor Room S-4900
U.S. Environmental Protection Agency
2777 South Crystal Drive
Arlington, VA 22202

Please let me know if you have any questions or need further clarification.

Thanks,

Keri

Doug Spilker
<doug.spilker.b@
bayer.com>

09/15/2008 12:32
PM

To
Keri Grinstead/DC/USEPA/US@EPA
cc
Subject

Inert determination - Non-Food uses

Hi Keri,
It was good to talk with you this morning. Thanks for the guidance on how to proceed with our questions. Please find below two inert ingredients we would like to use in a NON-FOOD USE product. Would you please check to see if these can be used, and if not - would you please provide us with guidance on what we would need to provide to EPA to get these approved for NON-FOOD USE by EPA?

Again, if I can do anything to facilitate getting the information you need to evaluate [redacted] please do not hesitate to call.

Thanks,
Doug

1. [redacted]
2. [redacted]

Doug Spilker, Ph.D.
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

Attachment 3

Doug Spilker/SHAWN/AGCHEM/US/BAYER

04/13/2009 10:49 AM

To alexander.bewanda@epa.gov

cc Lisa Lowseth/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES, Bruce Martin/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

bcc Mary Hunt/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Jagdeep Buch/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Douglas Hutchens/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

Subject Minutes of Pre Reg Meeting (03/30/09) - Collar - Acute Toxicity Requirements

Dear Ms. Alexander,

One of the action items from the Pre-registration meeting (subject - Acute Toxicity Requirements) of March 30, 2009 between Bayer Animal Health and the Agency was for us to prepare and submit meeting minutes containing our understandings from the meeting. Therefore, please find attached the respective minutes from the subject meeting, and the attachment we used during the discussion.

We ask for the Agency's review and concurrence that our understandings from the pre-registration meeting are correct. If there are any misunderstandings or inaccuracies, we ask that you let us know as soon as possible.

Best regards,

Doug

Doug Spilker
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

Questions for EPA - acute toxicity March 30 2009.doc EPA Mtg 2009 Mar 30 Flu + Imid Collar Acute Tox.doc

Bayer HealthCare
Animal Health Division

Bayer HealthCare LLC
Animal Health Division

Date: April 13, 2009 File Reference: EPA Mtg 2009 Mar 30 Flu + Imid Collar Acute Tox.doc

Subject: Teleconference between Bayer Animal Health and EPA - Insecticide/Rodenticide Branch & Technical Review Branch, March 30, 2009; Proposed Acute Toxicity Requirements for Flumethrin + Imidacloprid Collar

From: Douglas A. Spilker, Ph.D. Phone: 913-268-2751

To: Ms. BeWanda Alexander EPA, Registration Branch (Team 13)

Attendees: EPA (Agency) – BeWanda Alexander, Richard Gebken (PM), Byron Backus (TRB)
Bayer Animal Health (BAH) – Lisa Lowseth, Rex Henry, Bruce Martin, Mary Hunt, Jagdeep Buch and Doug Spilker

A. Purpose of Meeting

The teleconference and discussion basically followed the handout order (see attached document, 3 pp.). The purpose of this meeting was to discuss with the Agency the study/data requirements to support the submission of an application for registration of a flumethrin + imidacloprid combination dog/cat flea and tick collar. Acute toxicity data requirements/protocols for a spot on formulation were previously discussed in a Pre-registration meeting with the Agency on October 11, 2006. However, due to the change in proposed formulation from a spot-on to a collar, this additional discussion was warranted due to the fact that some of the studies might not be possible due to the nature of the active ingredient and/or formulation. Please find below Bayer Animal Health's understandings from the meeting, and the request for the Agency's concurrence on these points.

B. Data to Support Imidacloprid TGAI

BAH will receive authorization from Bayer CropScience to cite the toxicity data on imidacloprid TGAI previously submitted and accepted by the Agency.

C. Data to Support Flumethrin TGAI

There are limitations in the conduct of acute toxicity studies due to physical characteristics of the TGAI [glass-like solid at 20°C; difficulty in accurately measuring small quantities for dosing unless material is heated and diluted.]

1. Acute Ocular irritation in rabbits

BAH asked whether EPA would entertain a waiver request for the requirement of a primary eye irritation study with flumethrin TGAI. Due to the physical characteristics of the TGAI, it is not possible to accurately remove a 0.1 ml or 100 mg sample per OPPTS 870.2400 for placement in the conjunctival sac. Flumethrin must be heated to 60-70°C to form a liquid which can then be mixed with an appropriate vehicle such as corn oil for more accurate dosing.

BAH conducted an acute ocular irritation study in rabbits with flumethrin at a concentration of 10% in olive oil (1994, according to OECD 405, EPA 798.4500 and 81.5). In this study, the AI was not an ocular irritant.

Agency Response: No firm commitment was made from the Agency regarding the granting of a waiver for this requirement. Dr. Backus recommended we try a cryogenic grinding method for the TGAI, and observe whether the TGAI stays finely ground, or whether it reverts to the original amorphous phase. If the testing shows that it reverts to the amorphous glass-like phase then the study does not seem feasible. BAH should try this, and then discuss it again with Dr. Backus. Under these circumstances, a waiver might be possible.

We only need to submit the previously conducted study using 10% flumethrin in olive oil if we find it useful as background information.

2. Acute dermal Irritation in Rabbits

BAH would like concurrence from the Agency regarding a modification of the acute dermal irritation study with flumethrin TGAI.

BAH recently (2008) conducted an acute dermal irritation study in rabbits with flumethrin diluted 50% in corn oil. Flumethrin was warmed in a water bath to 66°C, diluted 50% with corn oil, cooled to RT and 1.0 ml of this mixture used for the dermal dose. The 0.5 ml of TGAI was still administered per OPPTS 870.2500. Results: slight erythema only at 1 hr post-dressing removal; assigned to Toxicity Category IV.

Agency response: This study is reasonable, and conforms to variations allowed by the guidelines for conduct of such studies.

D. End-Use Product – Collar

BAH planned to request a waiver of 5 of the 6 studies required for the end-use product similar to what was done for the cattle ear tags, due to physical characteristics of the collar (solid plastic material). BAH will conduct an acute dermal irritation study with the final collar product. The studies for which a waiver was planned included:

- Acute oral toxicity
- Acute ocular irritation
- Acute dermal toxicity
- Dermal sensitization
- Acute inhalation

Agency response: This plan is reasonable except for the omission of the dermal sensitization requirement. A dermal sensitization study should be conducted using ground collar material (may be frozen and then ground). Furthermore, the Agency asked that we include information on the release rate of the active ingredient from the collar in our justification for the waiver of the acute oral toxicity data requirement.

E. Consideration of testing with Reflector Device (components = clip and reflector)

The reflector [device] is made of two components: 1) Clip material – Makrolon® (polycarbonate) and 2) Reflector material - polymethyl-methacrylate. Neither component contains any pesticide.

BAH proposes that no toxicity testing is needed for the reflector.

Agency response: This plan is acceptable since the reflector is a device, will not be a part of the collar in the package (i.e. in separate bag), and contains no active ingredients. Furthermore, the aforementioned studies should be conducted without the reflector, this being considered the worse-case scenario in that the reflectors *might* reduce AI release.

F. Action items/EPA Guidance

BAH should prepare minutes for the Agency's confirmation of the understandings from this teleconference, and send via Ms. Alexander for distribution within the Agency.

For submission with the Application for Registration, each waiver request should be prepared as a stand alone document, with its own report number and formatted according to PRN 86-5. This is so that each requirement is addressed separately and has its own MRID number (for tracking purposes.)

Attachment:

"Questions for EPA – acute toxicity March 30 2009.doc"

Das 041309

Information for Discussion
Bayer HealthCare, LLC Animal Health (BAH) and EPA Teleconference March 30, 2009 at 11:00 AM (eastern)

RE: Acute toxicity testing of flumethrin technical grade (AI) and end-use product – flea/tick collar for use on puppies/dogs and kittens/cats

Background:

PowerPoint presentation made by BAH to EPA on October 11, 2006 - BAH requested that the Agency waive the acute ocular irritation study in rabbits and the acute dermal irritation study in rabbits due to the physical limitations posed by flumethrin (glass-like solid at 20°C).

Original discussion was for a spot-on for flea/tick control product with flumethrin, which has been discontinued.
The new product under development is a plastic collar with flumethrin and imidacloprid as AIs.

Flumethrin will be a new AI registration. Imidacloprid is currently registered.

Items for Discussion March 30, 2009

1. Flumethrin TGAI

1.1. Physical Characteristics

Limitations due to physical characteristics of the TGAI:

- Glass-like solid at 20°C
- Difficulty in accurately measuring small quantities for dosing in acute ocular and dermal irritation studies unless material is heated and diluted

1.2. Acute Ocular irritation in rabbits

BAH would like concurrence from the Agency that a waiver will be granted for the requirement for a primary eye irritation study with flumethrin TGAI. Due to the physical characteristics of the TGAI, it is not possible to accurately remove a 0.1 ml or 100 mg sample per OPPTS 870.2400 for placement in the conjunctival sac. Flumethrin must be heated to 60-70°C to form a liquid which can then be mixed with an appropriate vehicle such as corn oil for more accurate dosing.

BAH conducted an acute ocular irritation study in rabbits with flumethrin at a concentration of 10% in olive oil (1994, according to OECD 405, EPA 798.4500 and 81.5). In this study, the AI was not an ocular irritant.

Is this acceptable to the Agency?

1.3. Acute dermal Irritation in Rabbits

BAH would like concurrence from the Agency regarding a modification of the acute dermal irritation study with flumethrin TGAI.

BAH recently (2008) conducted an acute dermal irritation study in rabbits with flumethrin diluted 50% in corn oil. Flumethrin was warmed in a water bath to 66°C, diluted 50% with corn oil, cooled to RT and 1.0 ml of this mixture used for the dermal dose. The 0.5 ml of TGAI was still administered per OPPTS 870.2500. Results: slight erythema only at 1 hr post-dressing removal; assigned to Toxicity Category IV.

Is this acceptable to the Agency?

2.0 End-Use Product – Collar

2.1 BAH requests a Waiver of 5 of the 6 studies required for the end-use product similar to what was done for the cattle ear tags due to physical characteristics of the collar (solid plastic material)

- Acute oral toxicity
- Acute ocular irritation
- Acute dermal toxicity
- Sensitization
- Acute inhalation

BAH will conduct an acute dermal irritation study with the final collar product.

Is this acceptable to the Agency?

2.2. Consideration of testing for Reflector Device (components = clip and reflector)

Clip Material: Makrolon® (polycarbonate)

Very stable material, widely used
Used in medical devices such as corrective eyeglasses and needle-less syringes, water bottles, protective head gear for sports, vehicle headlights

Reflector Material: polymethyl methacrylate

Very stable material, widely used
Used in medical devices such as intraocular lenses and orthopedic implants, toys, glazing on aircraft, lenses, light pipes

The Reflector Device does not contain any pesticide active ingredients.

BAH proposes that no additional toxicity testing is needed for the reflector.

Does the Agency concur?

Attachment 4

Minutes from US EPA Bayer–Animal Health Division Pre-R tration Meeting
for Flumethrin Technical and Flumethrin Combo Products
September 14, 2006

Meeting Attendees

Bayer	*EPA*		*Exponent*
Terry McNamara	George LaRocca	RD/IB	Jim Messina
Ulrich Heukamp	Bewanda Alexander	RD/IB	
Wendell Davis	Kevin Sweeney	RD/TRB	
Mary Hunt	Shyam Mathur	RD/TRB	
Doug Spilker			
Anja Hoelscher			
Bob Arther			

Meeting Purpose

Describe new products; agree on data requirements; streamline registration process; defer discussion on toxicology/human safety and domestic animal safety data requirements.

Agenda/Powerpoint Presentation

Generally, the powerpoint presentation was followed and speakers described their respective portions of the presentation. Copies of the presentation and the draft label were distributed (both attached).

Description of Products
Terry McNamara began the presentation, describing the products. Powerpoint slides 1-5.

World Wide Status of Flumethrin
At slide six, Ulrich Heukamp began explaining the established, world wide use of flumethrin in a variety of products (slide 7).

- Bob Arther clarified why Bayer had not pursued a flumethrin registration previously. Coumaphos has been used successfully in U.S. livestock applications, and Bayer U.S. could not justify the time and expense to develop and register flumethrin for livestock uses. However diseases carried by ticks have lately become a greater concern, the companion animal market is large, and flumethrin combined with imidacloprid represents an attractive flea and tick product for companion animals.

- George LaRocca pointed out that if the product works systemically, it would be considered an FDA regulated drug. Bob Arther explained that flumethrin is not systemic, but behaves like other pyrethroids, such as permethrin. In Europe the regulatory authorities do not distinguish between pesticides and drugs; all animal products are considered veterinary medicines.

- Ulrich Heukamp continued the program with his discussion on isomers. At this time, Shyam Mathur said he prefers the product labels to identify the amounts of the two Z

isomers. This can be a: atio of the two Z isomers –Z1 and Z2 s a listing of a percent for each.

- The Agency asked about the nominal percent active ingredient for the TGAI/MUP product. Bayer U.S. is currently working on this and agreed that the final claim will be based upon these analyses.

- On slide 15, any impurity listed on the Confidential Statement of Formula should be listed by chemical name and CAS number (if available) and all impurities greater than 0.1% must be listed. All impurities can be listed, but those greater than 0.1% must be listed. Any impurity of toxicological significance must be listed regardless of the level.

- The estimated submission timeframe was discussed. Bayer U.S. estimates a submission to EPA during the first quarter 2008 (calendar year).

Description of Spot-on Products and Flumethrin Spot-on
Wendell Davis began his portion of the presentation, demonstrating how to open a tube and administer the product (the tube contained water, slide 16).

Data Requirements
Terry McNamara began the discussion on data requirements. George LaRocca agreed that cat/dog use is considered an indoor residential use pattern (slide 23).

- For Product Chemistry, since the TGAI will be registered as an MUP, storage stability/corrosion characteristics and stability must be done with the MUP.

- George LaRocca agreed that no Environmental Fate hydrolysis study would be required (slide 29). This is based on the understanding that no manufacturing of the TGAI/MUP will occur in the U.S.

- George LaRocca emphasized the Agency's concern with technical product is with shipment within the U.S. For example, such data would be helpful if there is a spill of technical material within the U.S. Both George LaRocca and Kevin Sweeney agreed that there is no environmental exposure concern for the technical since it will not be manufactured or imported to the U.S. for formulation. Therefore the Ecological Effects studies should not be required. However, George LaRocca will review this with EFED and respond to Bayer.

Product Performance/Efficacy
Wendell Davis began the product performance portion of the presentation, describing the product and dose sizes (slide 38).

- There was much discussion regarding the label claim for waterproof (vs. water resistant). It was obvious this has been a significant discussion item within EPA. George stated he would never allow a waterproof claim. It seems there is variation among currently registered product labels. Bayer U.S. confirmed that Frontline Plus has the waterproof claim approved on its label. It was agreed that data will need to be submitted to support the claim. Kevin Sweeney acknowledged that if other products have the claim, EPA must treat all products in the same manner.

- George LaRocca asked about exposure of pets to water/bathing. Following exposure, what keeps the product on the dog? Terry McNamara responded that it was a result of the chemical properties of pyrethoids and the natural oils of the animal.

- The Agency said that the 12-hour efficacy claim may be an issue. Bayer U.S. explained that this claim is supported by data. Additionally, the Agency approved it for Advantage. EPA stated that it is probably not an issue if they have already approved the language for another product, although they will need to review the product specific data.

- Kevin Sweeney asked if 1.2 ml provides sufficient efficacy for big cats (>10 pounds). Bayer U.S. confirmed that it does and the same is true for large dogs.

- Kevin Sweeney asked about the *Ixodes scapularis* studies (slide 42). At this time, Bayer is planning *in vitro* hair laboratory studies. Kevin Sweeney will review the type of studies (*in vitro or in vivo*) which have been used in recent years to register products, and inform Bayer if the testing regime is acceptable.

- Kevin Sweeney is interested in reviewing dose titration studies for flumethrin and synergist. How was the amount of flumethrin used in end product determined? The study(ies) can be non-GLP. As the combination product contains flumethrin and MGK 264, a pyrethroid synergist, these studies should be with both flumethrin and the synergist. He prefers "spot on" study(ies) in the target animals, and not applications in other species. This will be submitted by Bayer as a supplemental study(ies) included with the submission package.

Finally the group summarized data requirements as follows:

Environmental Fate – no studies per George LaRocca.
Ecological Effects – possibly no studies; George LaRocca will review with EFED and inform Bayer.
Product Chemistry – ratio of Z isomers on product labels, and MUP (=TGA1) storage stability/corrosion characteristics and stability studies.
Efficacy – *Ixodes* study – need to determine *in vitro* or *in vivo*. Kevin Sweeney will review and inform Bayer. Prefer no European species of ticks.

<u>Draft Label</u>
Bewanda Alexander asked that we include the word "may" in regards to ticks carrying or transmitting disease. Also, it was requested that we include the statement "Do Not Rub In" on the product label.

Kevin Sweeney said that generally the Agency doesn't allow time of kill claims on labels, however if a claim is already approved on another label, then there should be no problem. For example, "Kills 98-100% of the adult fleas on dogs *within 12 hours* and continues to prevent infestations for at least four weeks."

Next meetings between US EPA and Bayer Animal Health were proposed for Wednesday, Oct. 11th. Possibly morning and afternoon meetings; one for Toxicology/Human Safety and another for Domestic Animal Safety to determine data requirements for registration.

List of Items for Agency Concurrence

- Use Pattern

  Under current 40 CFR Part 158 Appendix A, dog and cat uses are Indoor.

  Under draft 40 CFR Part 158 proposal dog and cat uses would be Indoor Residential.

- No data requirements (based on only dog and cat end-use products) for

  - Spray drift (40 CFR Part 158.440)
  - Plant protection (40 CFR Part 158.540)
  - Non-target insect (40 CFR Part 158.590)
  - Residue chemistry (40 CFR Part 158.240)

- Product Chemistry

  - Data requirements for MUP and EP clearly defined in 40 CFR Part 158
  - As the flumethrin TGAI will be registered as a MUP, storage stability/corrosion characteristics and stability must be done with the TGAI.
  - The amounts of the two Z isomers must be specified on the label as a ratio or listing of each.

- Environmental Fate

  Under current 40 CFR Part 158, no data should be required.

  Under draft 40 CFR Part 158, only 835.2120 Hydrolysis data are conditionally required under certain conditions, but these conditions are not similar to dog/cat use. Moreover, flumethrin does hydrolyze in similar manner as pyrethroids; a new hydrolysis study would provide little new information.

  Therefore no environmental fate data should be required.

- Ecological Effects
  Based on the use pattern (registration of a MUP for Indoor Residential Use), Bayer proposed

  850.2100 Avian oral toxicity (bobwhite)
  850.1075 Freshwater fish (both rainbow trout and bluegill)
  850.1010 Freshwater invertebrate (Daphnia)

  However the MUP will be made in India and shipped to Germany for formulation into the End Use Product (Spot On). The Spot On product is what will be imported into the U.S. Based on this, the MUP will not enter the U.S.; consequently, there will be no environmental exposure with the MUP, and these studies may not be necessary. George LaRocca will obtain an Agency decision on this.

- Efficacy

  - Flea (adult and larvae) efficacy will be supported by imidacloprid studies on file with EPA
  - Flea ovicidal (egg) efficacy will be supported by pyriproxyfen studies on file with EPA
  - Tick efficacy to support a general tick claim will be demonstrated by new GLP studies:

    - *Dermacentor variabillis* (American Dog Tick) conducted in dogs
    - *Rhipicephalus sanguineus* (Brown Dog Tick) conducted in dogs
      - Laboratory (*in vitro*) studies for immature life stages
    - *Amblyomma americanum* (Lone Star Tick) conducted in cats
    - *Ixodes scapularis* (Deer Tick)
      - Laboratory (*in vitro*) studies for all life stages
    - Bathing/Water studies to support waterproof claim for dogs
      - Bath group – weekly infestations and counts with one bath approximately 2 weeks post-treatment.
      - Water group – weekly infestations and counts, with weekly water immersions performed between counts and infestations.

Kevin Sweeney will review and respond.

Attachment 5

Doug Spilker/SHAWN/AGCHEM/US/BAYER

04/13/2009 10:00 AM

To alexander.bewanda@epa.gov

cc Jochem Rueter/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES, Rex Henry/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

bcc Bruce Martin/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Mary Hunt/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES; Jagdeep Buch/SHAWN/AGCHEM/US/BAYER@BAYER-US-NOTES

Subject Minutes of Pre Reg Meeting (03/24/09) - Collar - Product Chemistry Requirements

Dear Ms. Alexander,

One of the action items from the Pre-registration meeting (subject - Product Chemistry Requirements) of March 24, 2009 between Bayer Animal Health and the Agency was for us to prepare and submit meeting minutes containing our understandings from the meeting. Therefore, please find attached the respective minutes from the subject meeting, and the attachment we used during the discussion.

We ask for the Agency's review and concurrence that our understandings from the pre-registration meeting are correct. If there are any misunderstandings or inaccuracies, we ask that you let us know as soon as possible.

Best regards,

Doug

Doug Spilker
Manager - EPA Reg. Affairs
BAYER HEALTHCARE LLC
ANIMAL HEALTH
Office: +1 913-268-2751
Mobile: +1 816-506-3102
Fax: +1 913-268-2135
Email: doug.spilker.b@bayer.com

Address:
P.O. Box 390
Shawnee Mission, KS 66201-0390
Country: USA

Bayer Animal Health "Powered by People, Driven by Science"

EPA Mtg 2009 Mar 24 Flu + Imid Collar Prod Chem.doc

Flumethrin Isomer Ratio & Product Chemistry.pdf

Bayer HealthCare
Animal Health Division

Bayer HealthCare LLC
Animal Health Division

INTERNAL MEMORANDUM

Date: April 13, 2009 File Reference: EPA Mtg 2009 Mar 24 Flu + Imid Collar Prod Chem.doc

Subject: Teleconference between Bayer Animal Health and EPA - Insecticide/Rodenticide Branch & Technical Review Branch, March 24, 2009; Proposed Product Chemistry Requirements for Flumethrin + Imidacloprid Collar

From: Douglas A. Spilker, Ph.D. Phone: 913-268-2751

To: Ms. BeWanda Alexander EPA, Registration Branch (Team 13)

Attendees: EPA (Agency) – BeWanda Alexander, Richard Gebken (PM), Shyam Mathur (TRB)
Bayer Animal Health (BAH) – Rex Henry, Jochem Rueter, Bruce Martin, Mary Hunt, Jagdeep Buch and Doug Spilker

A. Purpose of Meeting

The teleconference and discussion basically followed the handout order (see attached document, 3 pp.). The purpose of this meeting was to discuss with the Agency the study/data requirements to support the submission of an application for registration of a flumethrin + imidacloprid combination dog/cat flea and tick collar. Product chemistry data requirements for a spot-on formulation were previously discussed in a Pre-registration meeting with the Agency on September 14, 2006. However, due to the change in proposed formulation from a spot-on to a collar, this additional discussion was warranted due to the fact that some of the studies might not be applicable due to the nature of the formulation. Furthermore, BAH requests additional clarification from the Agency regarding the expression of the isomer ratio of flumethrin on the label. Please find below Bayer Animal Health's understandings from the teleconference, and the request for the Agency's concurrence on these points.

B. Flumethrin Isomer Ratio Expression on Formulated Product Label (see page 1 of handout)

BAH presented several options for the label expression of the isomer ratio of the flumethrin component of the formulation. The Agency instructed that the label claim should appear as a maximum/minimum expression:

Trans Z-1/Trans Z-2 ratio: max 66% trans Z-1 and min 34% trans Z-2

C. Technical Material - Flumethrin Expression on Confidential Statement of Formula (CSF)

Only the nominal value of the flumethrin technical needs to be reported on the CSF for the flumethrin technical (TGAI); no isomers need to be itemized.

D. Formulated Product - Flumethrin Expression on Confidential Statement of Formula (CSF)

Only the nominal value of the flumethrin technical needs to be reported on the CSF for the flumethrin technical (TGAI); no isomers need to be itemized.

E. Physical and Chemical Properties Test Requirements for Formulated Product

In the list below is our understanding of the discussions from the teleconference for each of the study categories for the formulated product (collar):

Section and Title	Requirement
63-2 (830-6302) Color:	YES
63-3 (830-6303) Physical State:	YES
63-4 (830-6304) Odor:	YES
63-5 (830-7200) Melting Point:	N/A* (1)
63-6 (830-7220) Boiling Point:	N/A* (1)
63-7 (830-7300) Density, bulk density, or specific gravity:	YES
63-8 (830-7840) Solubility: (830-7860)	N/A* (1)
63-9 (830-7950) Vapor Pressure:	N/A* (1)
63-10 (830-7370) Dissociation Constant:	N/A*(1)
63-11 (830-7550) Octanol/water partition coefficient	N/A* (1)
63-12 (830-7000) pH:	YES; Request Waiver (2)
63-13 (830-6313) Stability:	N/A*(1)
63-14 (830-6314) Oxidation or reducing:	YES; Request Waiver -Will not act as an oxidizing or reducing agent
63-15 (830-6315) Flammability - flashpoint (combustible liquids only)	N/A*(3)

63-16 (830-6316) Explodability:	YES; Request Waiver (4)
63-17 (830-6317) Storage Stability:	Required (5) – Condition of registration; will provide after first production
63-18 (830-7100) Viscosity: (Liquids Only)	N/A*(6)
63-19 (830-6319) Miscibility: (emulsifiable liquids and is to be diluted with petroleum solvent)	N/A*(7)
63-20 (830-6320) Corrosion characteristics: (when packaged in metal, plastic or paper containers)	Required (8) – Condition of registration; will provide after first production
63-21 (830-6321) Dielectric breakdown voltage: (yes if for use around electrical equipment)	N/A*(9)
61-3 (830-1670) Formation of unintentional ingredients during manufacturing	YES; Discussion Required

* N/A = Not Applicable

1) Per 40 CFR 158.190 - This test is only required on Technical grade of active ingredient and not for end use product.

2) Per 40 CFR 158.190, This product is not soluble in water and pH of the test substance is not required.

3) Per 40 CFR 158.190; 63-15(a) - This product is not considered a combustible liquid, because the closed cup flashpoint for all the ingredients is greater than 199° F.

4) Per 40 CFR 158.190; 63-16(a) - This product does not contain any explosive ingredients.

5) Per 40 CFR 158.190; 63-17 - This is a study to support stability of the product in the market container. Stability is not part this study but will done under a separate study.

6) Per 40 CFR 158 190, 63-18. The product is a solid and viscosity is not applicable

7) Per 40 CFR 158.190; 63-19(a) - This product is not an emulsifiable concentrate type product.

8) Per 40 CFR 158.190; 63-20 - This is a study to support corrosion of the product in the market container and not part of his study but done under a separate study.

9) Per 40 CFR 158.190; 63-21(a) - This product is not intended for use around electrical equipment.

F. Consideration of testing with Reflector Device (components = clip and reflector)

The reflector [device] is made of two components: 1) Clip material - Makrolon® (polycarbonate) and 2) Reflector Material: polymethyl methacrylate. Neither component contains any pesticide active ingredients.

BAH proposes that no product chemistry information be required for the reflector.

Agency response: This is acceptable to the Agency since the reflector is a device, will not be a part of the collar in the package (i.e. in separate bag), and contains no active ingredients.

G. Action items/EPA Guidance

1) BAH should prepare minutes for the Agency's confirmation of the understandings from this teleconference, and send via Ms. Alexander for distribution within the Agency.

2) In addition to the paper copies, the storage stability information may also be submitted in electronic format (PDF or TIF files), but this is not a requirement.

3) The Agency reminded BAH that the enforcement method (Guideline No. 830.1800) should include both active ingredients (flumethrin and imidacloprid).

Attachment: Flumethrin Isomer Ratio & Product Chemistry.pdf

Das 041309

FOR OFFICIAL USE ONLY

FILE SYMBOL	
REGISTRATION NO.	11556-RLL

CONFIDENTIAL STATEMENT OF FORMULA ENCLOSED

DATE SUBMITTED	SUBMITTED BY (✓)	
	APPLICANT	BASIC SUPPLIER
SEP 27 2010		

Do Not Write Comments, Formula, or Parts of Formula on This Envelope

NOTE

It shall be unlawful—for any person to use for his own advantage or to reveal, other than to the Secretary, or officials or employees of the United States Department of Agriculture or other Federal agencies, or to the courts in response to a subpoena, or to physicians, and in emergencies to pharmacists and other qualified persons, for use in the preparation of antidotes, in accordance with such directions as the Secretary may prescribe, any information relative to formulas of products acquired by authority of Section 4 of the "Federal Insecticide, Fungicide, and Rodenticide Act."

Pages 224-233-*Confidential Statement of Formula may be entitled to confidential treatment*